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RADIOLOGY

EDITORIALS

Guest Editorial — *Bernard Shapiro, M.D.* 89

ARTICLES

Rectilinear Scanning — *W. F. P. Tuer* 92

Abdominal Angiography — *D. Graeb* 96

Angiography in the Diagnosis of Pulmonary Embolism — *A. Abubakare* 102

Hysterosalpingography — *S. Levinoff* 105

Radiation In Therapy — *M. Ho* 109

FEATURES

Symptomatology — *B. W. Malcolm* 108

Clinicopathological Conference — *H. Newman* 113

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Guest Editorial

Radiology - A Specialty With Unlimited Horizons

DR. BERNARD SHAPIRO was born in Montreal, Quebec and received his Primary and Secondary education in that city. In 1937, he entered the Arts and Science Faculty of McGill University and in 1940, the Faculty of Medicine at the same University. He received his Bachelor of Science Degree from McGill in 1942, and Medical Degree in 1943. Following his internship, he was commissioned in the Royal Canadian Army Medical Corps and served with the Canadian Army until 1946. In 1946, he became resident in Medicine at the Jewish General Hospital in Montreal. He was then resident in Radiology at that hospital and at Queen Mary Veterans' Hospital in Montreal, and attended the lecture course in Radiology at the Royal Victoria Hospital in Montreal. In 1950, he was certified by the Royal College of Physicians and Surgeons of Canada in both Diagnostic Radiology and Therapeutic Radiology. In 1951, he was appointed Chief of Service in Radiology at Westminster Hospital in London, Ontario and Consultant in Radiology for the District. He was also Associate in Radiology in the Faculty of Medicine at the University of Western Ontario. Since 1955, he has been Chief of Radiology and Nuclear Medicine at Mount Sinai Hospital in Toronto, and Radiologist-in-Chief at Baycrest Hospital. He obtained his Fellowship in Diagnostic Radiology in 1960, from the Royal College. Dr. Shapiro is an Associate Professor of Radiology in the Faculty of Medicine at the University of Toronto.

Radiology combines the aspects of an art, in which each patient must be considered an individual problem, with various clinical characteristics which must be taken into account, and a science, in which much definite information is available. Training in clinical medicine affords the radiologist the opportunity to perform the first function. His specific training in the field of Radiology allows him to achieve the second.

The first 50 years following the discovery of x-ray by Roentgen, were followed by slow acceptance by the Medical Profession of this new diagnostic and therapeutic tool. The specialty of Radiology slowly gained in stature. Many brilliant men contributed to the development of this as a *bona fide* specialty respected by all physicians. However, since the end of the Second World War in 1945, very rapid advances in the specialty of Radiology have taken place. There has been a concomitant increase in interest in the field by physicians and many young men have chosen this as their field of endeavour. The main reasons for the rapid advance of the field have been the following: (1) The advent of image intensification (2) Improved contrast materials (3) The marked proliferation of interventional Radiology (4) The rapid advance of Nuclear Medicine and (5) Improved programs of training in Radiology, both undergraduate and graduate.

1. IMAGE INTENSIFICATION AND TELEVISION CHAIN

This has become the norm for use during any fluoroscopic procedure. No longer is the radiologist encumbered by wearing red glasses and accommodating for 10 - 12 minutes prior to fluoroscopy. The examination does not have to be carried out in a darkened room. The image presented is bright and clear, and one can identify anatomical structures with great clarity. One can easily visualize the advance of a catheter in a vessel, study the motility of the intestinal tract, the urinary tract, and visualize contrast materials in the subarachnoid space, both in the spinal cord and the brain. All of these can be recorded on spot films, cine film or video tape for later study in detail.

2. CONTRAST MATERIALS

Many improvements in contrast materials have been made and we are now provided with safe intravenous materials (a) for cholangiography, (b) for excretory urography, (c) for the various vascular studies which are now so common.

3. INTERVENTIONAL RADIOLOGY

In 1952, Seldinger described a method of carrying out percutaneous catheterization of the femoral artery. By the use of the image intensifier, one can then follow a catheter into the aorta and also do selective catheterization of such vessels as the renal, superior mesenteric, coeliac, and the subclavian; the vertebral, carotid and coronary arteries. The combination of image intensification television viewing, improved contrast materials and the Seldinger method, has resulted in a vast proliferation of procedures that can be done with a very minimal amount of morbidity. Most University departments of Radiology now spend a great deal of their time performing these interesting, but very time-consuming studies. In addition to these vascular procedures, radiologists are called upon to do many other studies such as lymphangiograms, bronchograms, sialograms, myelograms, air encephalograms, discograms, lung biopsies, and so on. This variety of interventional studies adds interest to the specialty and also results in vastly improved diagnoses.

4. NUCLEAR MEDICINE

In view of the fact that the radiologist was familiar with the use of radium and x-rays and the hazards of radiation, it was natural for many of them to become extremely interested in the new specialty of Nuclear Medicine. Many departments of radiology sponsored the development of Nuclear Medicine in their own hospitals and have contributed greatly to this new and most interesting specialty. The use of radionuclides in diagnosis, especially in diagnostic scanning, increases continuously year after year. This is one of the newest and brightest divisions in the field of radiological science.

5. ACADEMIC RADIOLOGY

The radiologist is increasingly in demand as a teacher, both for graduate and undergraduate students. In our own university, the radiology departments are heavily involved in the Period III training, not only during the week that each clerk spends in the department, but during his entire period of training in other specialties. The radiologist has also been called upon to provide teaching in Period II and during Period I. The latter is of extreme interest, as utilizing a person who is clinically involved in the teaching of anatomy will only tend to heighten the interest of the first year student.

During the postgraduate period, every radiology department has a program of radiology conferences and seminars for the interns and residents of the hospital. There are also ward rounds and interdepartmental conferences. In addition to all this, the radiologist has to provide an active and concentrated program of teaching for residents in radiology.

SUBSPECIALIZATION IN RADIOLOGY

It is said that medical knowledge is increasing at the rate of 9% each year. This holds true for the field of Radiology as well. It is virtually impossible for any one person to assimilate the fund of knowledge available. We find that there are now subspecialists in the fields of Nuclear Medicine, Neuroradiology, Vascular Radiology, Therapeutic Radiology, and to a lesser degree radiologists with special interest in gastrointestinal radiology, renal radiology and so on.

The undergraduate should mainly become oriented in radiological methods (of diagnosis and treatment) and should acquire some insight into the enormous scientific possibility of the field. For the postgraduate student in radiology, a fascinating field is available in which he is in continuous contact with almost every other specialty in Medicine. He will still have considerable patient contact. For those who desire it, there is also great opportunity for teaching and the sorely neglected field of basic research in radiology. The horizons are unlimited for those who choose to specialize in the radiological sciences.

Editorial

A tense, haggard, overworked surgeon cannot understand why Mr. White's newly created anastomosis is not functioning. A harried obstetrician cannot decide whether it will be a single or double delivery for Mrs. Jones and why poor Mrs. Cohen cannot have any children at all. Does Mr. Lee's chest film show a pulmonary embolus or congestive heart failure? Is Mrs. Fortanelli's abdomen protuberant because of spaghetti or spleen? Does Baby Boy Blue have an aspiration pneumonia or respiratory distress syndrome? Is young Mr. Pilkington's eccentric behaviour due to an organic brain lesion or schizophrenia?

Each of the above typical clinical questions can often be answered after performance of a standard radiologic examination. Specialists in almost every branch of medicine depend upon the radiologist for his expert opinion, just as the radiologist must keep an active interest in almost every subspecialty. How sophisticated radiology has become since the first experiments of Wilhelm Roentgen in 1895! There is presently no part of the human body so hidden that it cannot be explored or treated by special radiological techniques. Often a simple procedure obviates the necessity to perform a laparatomy on a seriously ill patient. A routine chest x-ray may provide an incidental and early diagnosis of a hitherto silent and potentially fatal disease process.

Because radiology is such a critical adjunct to diagnostic medicine, it is important for all of us dealing with patients to have an understanding of techniques used, and to exercise judgment in the selection of procedures best suited for gaining an insight into particular problems. It is the wish of the editors that this issue of the JOURNAL will serve to stimulate interest in radiology and to enlighten the readers regarding present day radiologic concepts.

S.N.L. and W.F.T.

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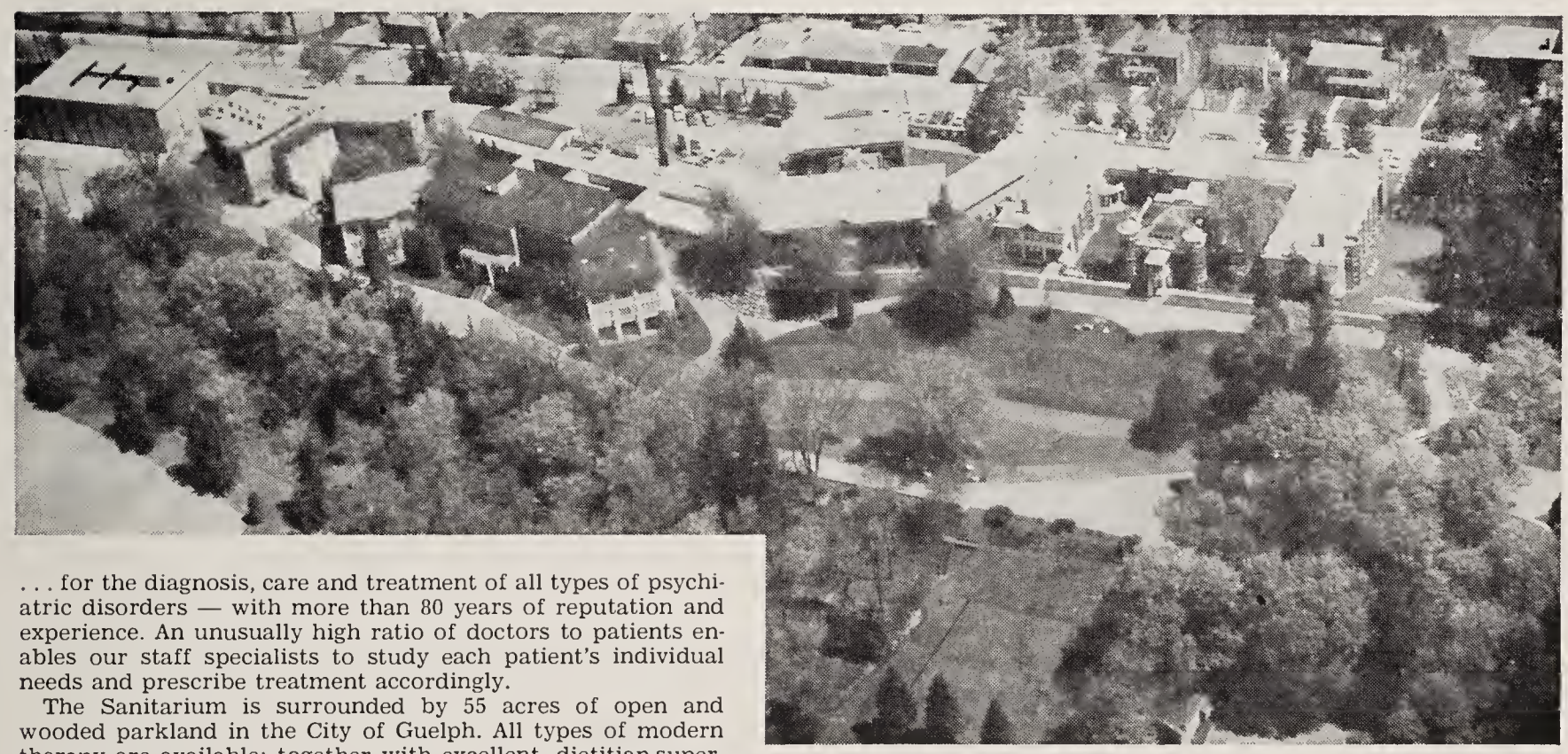

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Rectilinear Scanning

W. F. P. Tuer 7T0

INTRODUCTION

Scanning is the procedure of systematically mapping the distribution of radioactive substances in the human body. The method of scanning used most often in current clinical medicine is known as rectilinear scanning. Depending on the organ to be studied, and which function of the organ is of interest, a specific radionuclide is selected, and administered to the patient, usually intravenously. The selected radionuclide then accumulates in the desired organ. A directional gamma ray detector is moved over the subject in a pattern of parallel sweeps, and the picture appears as the information is received, analogous to the production of a single frame of a television picture, which is produced one line at a time.

Another common system is the scintillation camera, in which the entire field of the organ being studied is visualized simultaneously.

With each disintegration of the injected radioactive material, a gamma ray is emitted. In making a scan, one attempts to "count" the greatest number of gamma rays emitted from a series of overlapping units areas. A lead alloy collimator is placed between the source and the detector so that only those gamma rays which are parallel and coming from the region of the organ directly beneath the opening in the collimator are counted. "Filtered" gamma rays are absorbed by the detector, a thallium-impregnated sodium iodide crystal which is coupled to a series of photomultiplier tubes. The absorption of each gamma ray results in the emission of a number of light photons (scintillations) proportional to the energy of the absorbed ray. The energy of the photons is then amplified and converted to electrical energy by the photomultiplier tubes. The resultant electrical pulse has an amplitude proportional to the energy of the absorbed ray.

Because of this proportionality between pulse amplitude and gamma ray energy, one can set a threshold and/or upper limit of gamma ray energy to be recorded. This, in effect, varies the sensitivity and selectivity of the instrument. Once the unit responds to a gamma ray, by a series of integrated electrical circuits, it activates both a dot writer, which makes a mark on a piece of paper on top of the unit, and a light source which exposes a tiny portion of an x-ray film present within the unit. When the scan is completed, the x-ray film is developed in the ordinary fashion. Thus, two records of the scan can be kept.

Various physiological mechanisms are utilized in order to provide in the organ being studied a concentration of radionuclide sufficient to clearly outline the organ. These include the following:

1) *Active Transport*

By this mechanism, the cells concentrate the radionuclide against an electrochemical gradient. It is important in the accumulation of radioactive iodine used in thyroid scanning, Chlormerodrin in renal scanning, and Rose Bengal tagged with iodine, used in scans of the liver.

2) *Phagocytosis*

Liver scanning with colloidal gold employs the phagocytosis of gold by the reticulo-endothelial system.

3) *Cell Sequestration*

Red cells are labelled with Chromium 51, heated to damage them, and injected intravenously. The spleen then sequesters these damaged erythrocytes, and a splenic scan can be obtained from the gamma rays emitted.

4) *Capillary Blockade*

Iodine-labelled albumin is heated until the particles become large enough to occlude capillaries. When injected intravenously, they lodge in the lung and a scan is carried out.

5) *Diffusion – Simple and Exchange*

Radioactive mercury will diffuse into brain contusions, and similarly, radioactive selenomethionine is used for pancreatic scanning. In bone scanning, Strontium 85 is exchanged for calcium.

6) *Compartmental Localization*

An example of this mechanism is the placental scan, which is actually a measure of blood pooling.

APPLICATIONS

Thyroid Scanning

The value of the thyroid scan often depends upon the clinical acumen of the user. It does not completely solve the problem of which thyroid nodules to remove, but has spared many patients needless surgery. It cannot be a substitute for clinical judgment in thyrotoxicosis, but is often helpful in accurate diagnosis.

Patients for whom thyroid scan is indicated are the following:

1) Patients with suspected or proven cancer of the thyroid.

2) Patients who have solitary or multiple nodules, in which the diagnosis of benign disease is in question.

3) Thyrotoxic patients with nodular goitre.

The patient is given 20-40 microcuries of I^{131} by mouth on day 1. On day 2 he returns to the laboratory and the thyroid activity is measured. From this one can

calculate the thyroid uptake which is the percentage of ingested iodine accumulated by the thyroid. 12-32% is usually considered to be normal. In a thyrotoxic patient, the uptake is increased. This is a safe accurate method provided the patient has not had iodine recently for therapeutic or diagnostic reasons, such as gall bladder x-ray or intravenous pyelogram. After measurement of uptake, the patient has a thyroid scan in the normal fashion. Nodules are palpated and marked on the paper scan.

There is no scan pattern of the thyroid that is diagnostic of malignancy. "Cold" areas, that is, areas which take up less radioactive iodine than the surrounding thyroid tissue, may be benign but are usually malignant. If a nodule is "hot", if it is two centimetres or more in size, and if its margins are not well delineated by the scan, the chances that the lesion is benign are very high.

Bone Scanning

It has been shown that from 30-50% of a bone must be decalcified before a definite change can be demonstrated by x-ray. Often, metastatic lesions in the spine and lesions less than 1 cm. in diameter are not visualized on the x-ray at all. Bone scanning often proves to be more sensitive than x-ray in that it may both detect metastatic deposits before definite x-ray changes have occurred, and also delineate more clearly the lesion's boundaries. The latter is of great importance in planning radiation therapy for the patient.

Bone scanning, in which radioactive Strontium 85 accumulates in areas of increased activity, has proven to be of great value in the localization of bone lesions, including bone tumours, metastases, osteomyelitis, fractures, and Paget's disease. One normally sees osteogenic activity in the vertebral column, at the ends of the long bones, and in certain joints.

A dose of 100-200 microcuries for adults, and twenty microcuries for children is administered intravenously, and 24-48 hours later, the patient is scanned. During this interval, the body excretes up to 50% of the injected dose via the gastrointestinal tract and the kidneys, thus reducing the level of activity outside bony structures.

Before the scan is carried out, laxatives and enemas must be administered to ensure that any residual activity in the bowel is removed. Strontium 85 should not be administered to pregnant women or to children, unless there is a strong suspicion of a malignant bone lesion.

Pancreatic Scanning

Many agents with pancreas-localizing properties have been investigated in recent years. Until recently none has been found with sufficient localizing properties to permit specific visualization of this organ in a scan. It is now known that amino acids have a high degree of localization in the pancreas after the first few hours of administration, and their uptake into it is related to the synthesis of digestive enzymes. Further investigation has shown that methionine which has been treated so as to substitute radioactive selenium for sulphur takes place in the normal synthetic processes and serves as a suitable pancreatic marker. This agent has also been used to scan the prostate and parathyroid glands.

Se^{75}-L-selenomethionine is administered, and is quickly taken up by the pancreas. Since the liver picks up the radionuclide as well, two days later a liver scan should be done with colloidal gold, in order to outline the liver margin, so that a more definite idea of the extent of the pancreas may be obtained. Both a liver scan with colloidal gold 198, and a combined liver and pancreas scan with selenomethionine are done, and recorded on tape. One can then electronically subtract the liver scan from the combined scan and print out a pure pancreatic scan. This method is most promising, but as yet is done in very few departments of nuclear medicine.

The pancreatic scan has proven helpful in many cases in locating pancreatic tumours, which appear as "cold" areas, but failure to take up the radionuclide at present cannot be readily interpreted.

Lung Scanning

Lung scanning offers a new approach to the diagnosis of pulmonary disease. Workers have found that to date the most useful gamma-emitter for studying the lungs is radio-iodinated aggregates of human serum albumin.

Prior to scanning, the patient receives a saturated solution of potassium iodide to decrease the uptake of radioactive iodine by the thyroid gland. The patient inspires deeply in order to open basilar capillary beds; 200-300 microcuries of the compound are injected, and the scan is begun. With patient in the supine position, the scanning proceeds from the lower thorax to the apical region of the lungs. This direction is taken to prevent the progressive accumulation of radioactive iodine in the liver and spleen from obscuring the lower margins of the lungs.

It has been shown that the site of a pulmonary embolus may be demonstrated before any true infarction or radiographic change occurs. Since the embolism causes an obstruction of the pulmonary circulation, the area distal to the obstruction will show as a region of decreased perfusion on the scan. False positives may occur if there are localized pulmonary blebs which have gone undetected in routine x-rays. Angiography should be employed to delineate the precise site and extent of vascular obstruction when contemplating surgery.

Although areas of decreased or absent activity may occur due to bronchogenic carcinoma, pulmonary abscess, pleural scars, and pneumonia, the scan does not readily lend itself to differential diagnosis, and findings

must be interpreted in the light of the clinical picture, and with a radiograph of the lungs done at the same time.

Lung scans are easily done and take less than one hour. The method appears to be safe even in the critically ill patient. The use of the gamma camera has greatly reduced the time necessary to do lung scans, and allows four views to be taken — anterior, posterior and both lateral views.

The peripheral borders of the lung scan, especially in diaphragmatic surfaces, are difficult to interpret, because of the normal respiratory movement.

Splenic Scanning

Over the years, the spleen has proven to be an elusive structure to evaluate. Until recently, physical examination and plain films of the abdomen showing enlargement of the spleen directly or indirectly through changes in the outline of the bowel or stomach have been the methods used to observe the spleen. However, the development of a technique for scanning has made its visualization far more satisfactory.

The technique of sequestration of Chromium 51-labelled damaged erythrocytes by the spleen mentioned previously is used.

Scanning may be done in the prone, supine, or left lateral positions. Appropriate landmarks are put on the scan record, or one may take an abdominal x-ray in the same position, and superimpose the scan over the x-ray.

The scan of the spleen may never assume the importance of thyroid, liver, or brain scans, but it can be quite useful in the determination of splenic size, contour, change of size in response to medication, and as an aid in the differential diagnosis of a left upper quadrant mass. Since sequestration of the modified erythrocytes takes place only in functioning splenic tissue, a "cold" area suggests an area of dysfunction, such as a splenic cyst or tumour.

Liver Scanning

Liver scanning offers advantages in diagnosis that are not equalled by other methods. Accuracy of diagnosis has been found to be superior to that of alkaline phosphatase and BSP determinations. In one series of 548 cases of liver scans, abnormalities were detected in more than 80% of patients with space-occupying lesions, while liver function tests were abnormal in only 65%.

Two methods are commonly used in scanning the liver. The first employs the phagocytosis of radioactive colloid material, either Au^{198} or technetium-sulphur colloid, by the reticulo-endothelial system in the liver.

The other procedure sometimes utilized is based on the accumulation of I^{131} Rose Bengal within hepatocytes by an active transport mechanism. This material is rapidly cleared from the blood and excreted into the bile, then directly into the gallbladder and gastrointestinal tract. Therefore this procedure has found special use in attempting to differentiate extrahepatic from intrahepatic causes of jaundice. It is felt that in the intrahepatic cases, Rose Bengal will still be excreted into the G.I. tract, whereas in the extrahepatic, it may remain in the liver for a prolonged period (8 - 24 hours).

Colloidal gold studies will readily demonstrate metastatic deposits in the liver, if they are at least two centimeters in diameter, as areas of decreased activity. Liver scans are often done when an occult carcinoma is thought to exist in the liver, or in the presence of a known primary carcinoma elsewhere, to determine if there are metastases in the liver.

The main cause of error in the interpretation of the liver scan appears to be pressure by extrahepatic masses on the liver. Diffuse benign processes, such as fatty deposits or cirrhosis, can be suggested by correlation with the clinical findings and liver function tests. One also looks for increased uptake of the nuclide in the spleen and bone marrow in these cases.

Recently most laboratories have begun to use Technetium 99m as the radionuclide of choice. This has reduced the time required to carry out the procedure because scanning may begin one hour after injection of Technetium 99m.

Brain Scanning

One of the most commonly used, and useful scans, is that of the brain. For proper interpretation, one must be familiar with the anatomy and pathology of the intracranial vasculature.

Radionuclides used include Hg^{197} chlormerodrin, and Technetium 99m. Three to six hours following the intravenous injection of Hg^{197}, scanning may be done.

Increased activity is normally found on normal scans over the scalp, calvaria, and venous sinuses. Inferiorly, there is a large area of increased activity related to the vascularity of the facial musculature of and the nasopharynx.

Extracranial abnormalities may be visualized due to their increased blood supply. These include Paget's disease, hyperostosis, osteolytic lesions of the calvarium, and scalp oedema and hemorrhage. Most intracranial lesions appear as areas of increased activity in the scan. To interpret such an area as positive, an increased uptake should be visualized in two views. Lesions demonstrable by scanning include primary tumours of the brain, metastases, AV fistulas, subdural hematomas, abscesses, tuberculosis and cerebrovascular accidents. The latter are best visualized one week after the accident. It has been found that 70 - 90% of all brain tumours will have positive scans.

Renal Scanning

Renal scanning is a very useful means of assessing kidney function. The technique is simple, and no special preparation of the patient (such as dehydration, the administration of laxatives or enemas) is necessary. The renal scan can be used to delineate discrete areas of varied function within the same kidney. It may permit diagnosis of renal tumours, renal vascular disease, congenital abnormalities, or renal parenchymal disease.

In most cases, 200 microcuries of Hg^{197} chlormerodrin is administered intravenously and scanning is begun one hour later. The scanning process takes from 45 to 60 minutes. One notes the size, shape, position and distribution of radioactivity in each of the kidneys.

A patchy appearance occurs in a variety of renal parenchymal disorders, and may be present when other renal function tests are normal. This "salt and pepper" appearance is frequently seen in nephrosclerosis. Cold areas usually denote cysts, neoplasms, or abscesses, and may be seen on the scan if they are greater than three centimeters in diameter. If there is severe, bilateral impairment of renal function, the kidneys may not be visualized. Failure to visualize one kidney may be associated with arterial occlusion, or with extensive neoplasm.

One may also do a renal flow study with Technetium 99m and a gamma camera. Tumours will become opacified with radionuclide, cysts will remain as negative areas.

Placental Scanning

Accurate localization of the placenta is of great importance in the differential diagnosis of ante-partum hemorrhage, and is very helpful in localization prior to amniocentesis.

In placental scanning, there is minimal risk to either mother or fetus, and there is no operative procedure as in retrograde femoral arteriography.

Various materials may be injected. Until recently iodinated human serum albumin was injected intravenously. Ten minutes after injection an uptake study is done over the heart. The uterus is divided into twelve parts, scanned and each area is studied. The number of counts over the precordium is taken as 100%, and the activity over the other sectors is expressed as a percentage of this. Blood pooling in the area of the placenta will cause an increased number of counts, thus allowing accurate localization of the placenta.

Recently the method has been changed: isotopes such as technetium are injected intravenously, and 2 gamma camera views of the blood pool are obtained at right angles to each other. The accuracy remains the same but the speed of obtaining the information has been improved. The radiation dose to the fetus is about 1/200 of that with two x-rays of the abdomen.

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REFERENCES

1. Freeman, L. M.; Johnson, P.M.: *Clinical Scintillation Scanning*, Hoeber 1969.
2. Quinn, J. L.: *Scintillation Scanning in Clinical Medicine*, Saunders 1964.
3. Potcer, E. J., et al: J. Nuclear Medicine, 4:203, 1963.

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Abdominal Angiography

Douglas Graeb 7T1

INTRODUCTION

Angiography is the study of blood vessels in living subjects by the use of X-ray contrast methods. The arterial, venous and lymphatic circulations may be visualized on X-ray films, through the injection of radiopaque media into the appropriate vessels. The techniques are called arteriography, venography, and lymphangiography, respectively. Injection of radiopaque medium into the aorta (for X-ray study of this vessel and its branches) is called aortography. Selective arteriography is the introduction of radiopaque medium into one specific branch. This article will concern itself chiefly with the radiology of the abdominal aorta and its branches.

HISTORY AND PRESENT STATUS

On November 8, 1895, Wilhelm Roentgen accidentally discovered the phenomenon which he called X-rays. One month after the publication of Roentgen's discovery, Haschek and Lindenthal injected a radiopaque mixture into the blood vessels of an amputated arm, and produced a relatively high-quality X-ray photograph of the arteries and veins of the hand. In the course of the next 27 years many workers, by injecting radiopaque materials into the vessels of cadavers, were able to radiograph the blood vessels of almost every organ of the body in considerable detail.

Not until 1923 did anyone dare inject a radiopaque medium into the circulation of living humans. In that year Sicard and Forestier, after preliminary trials in dogs, injected radiopaque oil into the antecubital vein of human subjects. In 1929 a Portuguese surgeon, dos Santos, inadvertently punctured the abdominal aorta while performing lumbar ganglionic blockade. Apart from the pain involved, the complications of this manoeuvre were quite benign. Dos Santos went on to investigate and develop the technique as a practical method for visualizing the abdominal aorta.

Forssmann, one year earlier, had already proven the feasibility of catheterizing the heart by passing a catheter into his own ante-cubital vein and into the right atrium, so that by this time the main physical breakthroughs required for the development of angiography had been made.

The exploitation of the potential of angiography awaited the development of better, safer contrast media and of rapid film-changing techniques for multiple exposures, and advances in the technique of cardiovascular surgery over the ensuing twenty years, providing the stimulus for the development of angiography.

The chief value of angiography rests in its ability firstly to give a definite guide to the location of a vascular lesion, the condition of the vessels on either side of the lesion, and the development of collateral circulation and secondly, to aid in the differential diagnosis of abdominal masses.

TECHNIQUE & RADIOPAQUE MEDIA

X-rays are best absorbed by elements of high atomic weight. Virtually all radiopaque media in use are organic compounds with one, two or three iodine atoms on a six-numbered rings, e.g. Diatrizoate Sodium (Hypaque).

There are three essential qualities for such a medium: high opacity, low toxicity and ease of dissemination with blood.

Two main techniques have been used to introduce radiopaque media into the abdominal aorta. These are:

1) the *translumbar technique*

2) *retrograde catheterization* through the common femoral artery.

INDICATIONS & CONTRAINDICATIONS

Abdominal aortography is most frequently undertaken in anticipation of surgery designed to correct a vascular defect. The general indication of this procedure is any suspected disease of the abdominal aorta, its major branches, or an organ supplied by these branches. It is justified only when specific information is sought which cannot be obtained from a more benign clinical or laboratory examination. There is therefore, no point in submitting to this procedure patients whose general condition will not tolerate the operation and it is contraindicated in such a patient.

More specific contraindications include:

1) hemorrhagic diathesis or anticoagulant therapy,

2) known iodine sensitivity,

3) diffuse renal disease, with elevated BUN, albuminuria, or oliguria,

4) severe cardiac disease or recent myocardial infarction,

5) severe hypertension (systolic pressure greater than 250 mm. Hg) which predisposes to bleeding from the puncture site, and

6) severe liver disease (because of prolonged prothrombin time).

The dilemma which faces the clinician is that the patient who requires vascular surgery and is most likely to benefit from aortography also tends to suffer from

renal disease, cardiac disease, and/or hypertension. Indeed, the surgery is often intended to correct these conditions. Accordingly, the presence of these diseases is not an absolute contraindication to abdominal aortography. Considerable clinical judgement is required to evaluate the risks imposed by these conditions in each individual patient.

Below is a summary of specific indications for abdominal aortography:

A. *Diseases of the Abdominal Aorta*

I Congenital abnormalities, such as coarctation of of the abdominal aorta and aortic atresia.

II Acquired

1. Thrombo-occlusive disease (e.g. atherosclerosis, thrombosis, and embolism) resulting in incomplete or complete obstruction; e.g. the Leriche syndrome.
2. Aortic aneurysm
3. Dissecting aortic aneurysm

B. *Diseases of the Main and Secondary Branches of the Abdominal Aorta* (e.g. the coeliac, superior and inferior mesenteric, renal, iliac, and femoral arteries)

I Congenital disorders of these vessels

II Acquired

1. Atherosclerosis, causing signs and symptoms of relative or absolute ischemia (e.g. gangrene of bowel, hypertension of renal origin, and intermittent claudication)
2. Fibromuscular dysplasia of renal arteries
3. Aneurysm

C. *Diseases of the Organs Supplied by the Branches of Abdominal Aorta*

I Kidney

1. Hypertension of renal origin
2. Differential diagnosis of a space-occupying lesion of the kidney
3. Hydronephrosis
4. Renal malformations (e.g. aplasia, hypoplasia, horseshoe kidney, double kidney, polycystic kidney, ectopic kidney, etc.)
5. Assessment of potential renal function
6. Pre-nephrectomy investigation

II Adrenal Glands

1. Diagnosis of adrenal hyperplasia and adrenal neoplasia

III Pancreas

1. Detection of space-occupying lesions of the pancreas

IV GI Tract

1. Determination of site of acute bleeding
2. Mesenteric arterial insufficiency (e.g. abdominal angina, mesenteric infarction)
3. Mesenteric cysts
4. Mesenteric metastases

V Liver

1. Space-occupying lesion (primary or secondary neoplasm, cysts, etc.)

RADIOGRAPHIC FINDINGS

I. AORTA

a) Thrombo-occlusive disease

Investigation of thrombo-occlusive disease of the aorta and iliac arteries is the most common indication for abdominal aortography. Partial occlusion may be found even in the presence of good femoral pulsations. Since a significant number of patients complaining of intermittent claudication in the calf or thigh have been shown to have thrombo-occlusive lesions of the aorta-iliac system, this symptom constitutes an indication for abdominal aortography. Long-film angiography, in which films may be taken of the passage of a single injection of medium from the abdominal area to popliteal area, has been found valuable.

Normal vessels, when seen in an aortogram, have a characteristic appearance. Their walls are smooth and regular; their diameter tapers gradually and regularly as they approach the periphery of their distribution. The main-stem vessels run a straight or smoothly curved course. Visceral and parietal branches may be more tortuous.

In thrombo-occlusive disease, a wide variety of changes is noted. Narrowing and irregularity of the wall is commonly seen, or the vessels may be dilated and tortuous, with frank aneurysm formation. Calcification and filling defects may also be present. A decrease in the density of the opaque column indicates the presence of a mural thrombus or plaque on the wall. This may be revealed as a true stenosis on a lateral view. Many or all of these appearances are commonly seen on one film. Occlusion is the end stage of the disease process. Acute occlusion may be caused by embolism, and may not necessarily be related to an atherosclerotic process.

One of the most important changes seen with occlusion or severe stenosis, is the visualization of *collateral circulation*. Collateral vessels receive blood from a point proximal to the obstruction and distribute this blood to organs normally supplied by the diseased artery. They may also rejoin the the diseased artery at a point distal to the obstruction, where it is still patent. Experimental and clinical observations indicate that these vessels are probably present before the disease process begins but are quite small in the presence of normal major arteries. Hence they are seldom seen in the absence of occlusion.

Presumably tissue ischaemia, via a sympathetic nerve reflex, causes these vessels to dilate[1].

Collateral vessels may be recognized by the irregularity of their course, their inconstant distribution and their great numbers and proximity to each other.

Blood flow through a vessel may be relatively adequate until its diameter is reduced by 70 per cent or more[2]. This means that patients with any of the symptoms of intermittent claudication or the Leriche syndrome caused by chronic stenosis or aorta-iliac obstruction must be quickly recognized and assessed for surgical correction, for complete occlusion may occur relatively rapidly. The size and location of the obstruction, the adequacy of collateral circulation, and the condition of the vessels distal to the occlusion, are all factors which the surgeon must take into account in planning his therapy for the patient. This information is best gained by abdominal aortography.

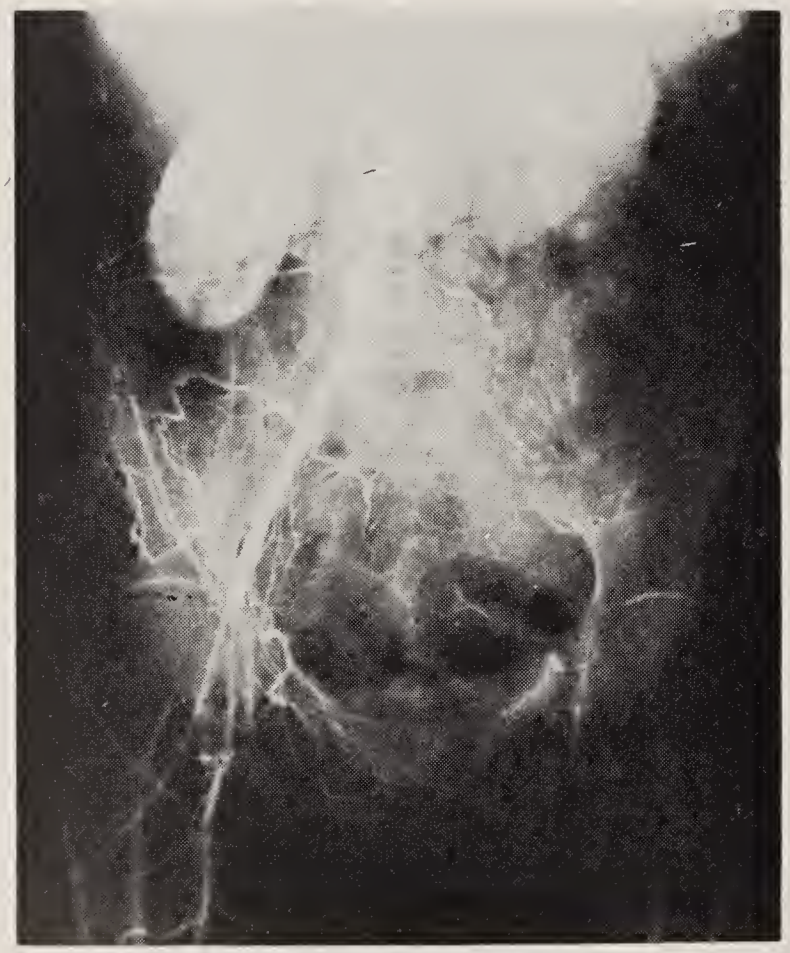

FIGURE 1—This patient was previously given a Teflon graft to replace the abdominal aorta and both common iliac arteries. The radiograph shows complete occlusion of the left iliac graft. The internal iliac and superficial femoral arteries are also occluded on the right. Many collateral vessels are seen. The few vessels which are seen on the patient's left are filled from collaterals on the right.

b) Abdominal aortic aneurysm

Abdominal aortic aneurysm is most frequently a complication of atherosclerosis of the aorta. Syphilitic aneurysm tends to occur more frequently in the thoracic aorta; the use of antibiotics has reduced the incidence of this condition in recent years. A relatively small number of aneurysms may be caused by infection (mycotic aneurysm), trauma or dissection of the media.

Aortic aneurysm is a lethal disease. Forty to eighty per cent of patients may die within one year of diagnosis if replacement by graft is not performed.

Aortography frequently establishes the diagnosis, and is valuable in a pre-operative assessment of the condition. However, aortography may be inaccurate in demonstrating the size and location of the aneurysm, because of the low pressure of blood through the dilated vessel, and the presence of mural thrombi. The dilated portion of the aorta is frequently coated with thick, laminated thrombus so that the opacified column of blood flowing through the thrombus-lined aneurysm may be little wider than normal. As previously mentioned, aortography is also considered slightly more dangerous in this condition.

Dilatation of the lumen, kinking of the aorta where the aneurysm joins more normal portions of the vessel, and calcification of the aortic wall (which may be seen on plain film) constitute the principal radiographic findings. Aortography may show the calcified wall to be separated from the lumen by a considerable thickness of radiolucent thrombus.

c) Dissecting Aneurysm

Dissecting aneurysm is less common and frequently is not recognized as dissecting in nature, even with the use of aortography. The classical "double-barreled" picture, produced by the dissecting column of blood surrounding the intra-luminal column of blood, is seldom seen.

II. KIDNEY

1. Hypertension of renal origin

Renal artery stenosis is the cause of a small percentage of cases of systemic hypertension. Hypertension secondary to renal stenosis is nevertheless important because it is one of the few causes of hypertension which may be corrected by surgery. This diagnosis may be confirmed by abdominal aortography. The causes of hypertension of renal origin include:

A. Congenital (infrequent)
   - (a) stenosis of renal artery
   - (b) abdominal aortic coarctation
   - (c) renal artery aneurysm

B. Acquired
   - (a) vascular
     - (i) atherosclerosis of renal artery or adjacent aorta
     - (ii) fibromuscular dysplasia
     - (iii) thrombosis or embolism of a branch of the renal arteries
     - (iv) necrotizing vasculitis (e.g. polyarteritis nodosa)
     - (v) trauma
     - (vi) compression of the renal artery by tumour, cyst, band, etc.
     - (vii) renal vein thrombosis

(b) parenchymal
  (i) hydronephrosis
  (ii) chronic pyelonephritis
  (iii) glomerulonephritis
  (iv) capsular hemorrhage
  (v) renal infarct
  (vi) chronic obstructive uropathy, and others.

Partial obstruction of the renal arteries may be a common denominator also in the *parenchymal* causes of hypertension. A thorough investigation of renal function is indicated in all cases of hypertension, including PSP excretion, split function studies, urography, pyelography, and renin assay in addition to abdominal aortography.

By far the most common causes of renal hypertension are atherosclerosis and fibromuscular dysplasia. These conditions may be unilateral or bilateral. The latter occurs most frequently in young adult women.

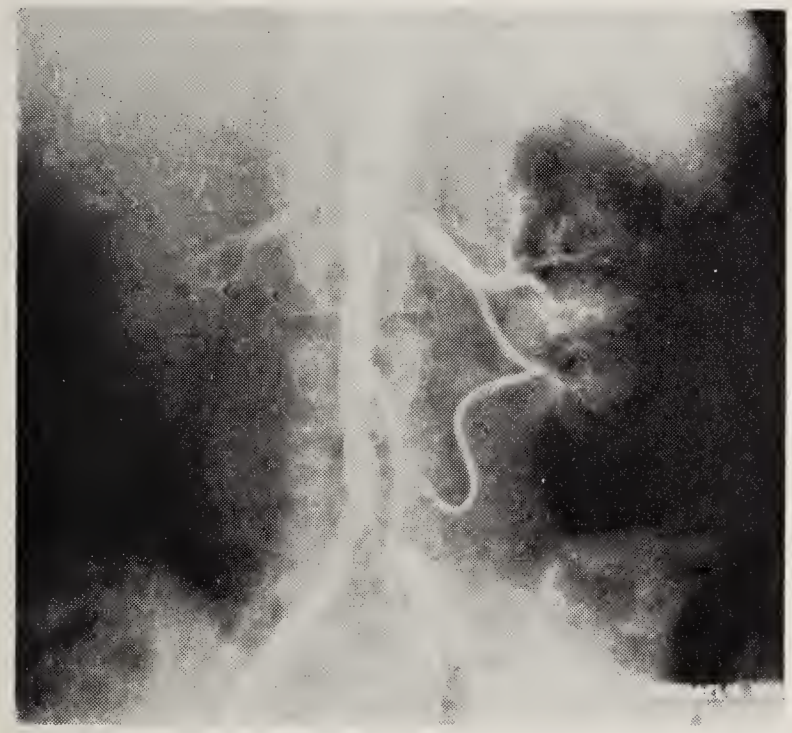

FIGURE 2—This aortogram shows typical atheromatous changes. The wall of the aorta and of its branches is quite irregular. There are stenoses near the origins of both the left renal and left common iliac arteries, with post-stenotic dilatation. The superior mesenteric artery is not seen, and is probably occluded at its origin. The large S-shaped branch of the inferior mesenteric artery is probably a collateral vessel supplying the distribution of the superior mesenteric artery.

The radiographic findings in atherosclerosis of the renal artery include segmental narrowing and post-stenotic dilatation of the proximal third of the main renal artery.

Fibromuscular dysplasia has a characteristically different radiographic appearance. Three types have been described. In *fibromuscular medial hypertrophy,* the most common variety, the main renal arteries have a beaded appearance. In *fibrous intimal stenosis,* the distal portions of the renal and segmental vessels are more uniformly narrowed. The *adventitial* form of the disease is rare.

In addition to the altered appearance of the arteries themselves, other abnormalities may be noted in association with renal artery stenosis. In the normal kidney, within about 10 seconds of the entry of the medium into the renal arteries, the whole mass of the kidney is seen to become uniformly opaque. This phenomenon, known as the *nephrographic phase,* is caused by the passage of the medium through the capillaries of the renal parenchyma.

Occlusion of a branch of the renal artery may cause a wedge-shaped area of non-opacification to be seen during the nephrographic phase. This appearance is diagnostic of renal infarct. Since kidney arteries are end arteries, there are no anastomoses to prevent infarction. The width of the cortex may also be decreased. This is a sign of renal ischaemia if other causes of parenchymal destruction can be eliminated.

2. Differential diagnosis of space-occupying lesion of the kidney

Selective renal arteriography is most useful in the differential diagnosis of a space-occupying lesion. By far the most common differentiation which must be made is between a malignant growth (i.e. renal cell carcinoma) and a non-malignant lesion (e.g. renal cyst, abscess, benign growth, hydronephrosis and others).

The advanced malignancy may be suspected on plain films, urography or pyelography, and nephrotomography. Nephrotomography is the simultaneous use of tomography and renal venography (the rapid injection of a large volume of contrast material into the renal vein producing opacification of the renal parenchyma). The use of tomography with venography allows the opacification of a thin section of the kidney to be viewed preferentially with blurring of all other areas. Nephrotomography is particularly valuable in demonstrating areas of increased vascularization, such as renal malignancy. Frequently, however, a small, round, well-defined renal mass will be seen on an IVP, and the differentiation is impossible without arteriography.

On arteriography, both the malignant and the non-malignant mass may be seen to displace normal renal vessels. The principal differentiating characteristic of renal tumours (and indeed of most tumours with a rich blood supply anywhere in the body) is the presence of *pathologic vessels.* These are seen in the arterial and early nephrographic phase. They are tortuous, irregular arteries forming frequent anastamoses with arteriovenous lakes. The tumour area is usually more opaque than the surrounding parenchyma. Sometimes avascular necrosis within the tumour occurs, causing radiolucent areas to be seen within the radiodense tumour.

The non-malignant mass, on the other hand, usually has a reduced blood supply, and therefore is seen as a radiolucent filling defect in the nephrographic phase. If the mass is a cyst which extends extrarenally, a raised border of renal parenchyma may be formed, causing a

characteristic *beaking* to be seen when viewed tangentially on the nephrogram.

The new vessels which grow into a malignant tumour may differ from normal vessels or vessels in a benign mass in a number of ways. There may be a deficiency in their muscular layer, or they may outgrow their nerve supply. Because of these and probably other factors, these vessels are unable to constrict in response to adrenaline. Injection of adrenaline through the catheter into the renal artery will cause constriction of normal vessels and vessels in a benign lesion. Vessels in a malignant tumour will be preferentially filled with blood. Injection of adrenaline will therefore cause these vessels to appear relatively wider than the normal constricted vessels on the arteriogram.

Areas of tumour involvement also exhibit early filling and late retention of the medium. Focal areas of opacity may thus be seen when the rest of the kidney is already relatively free of contrast material.

3. Hydronephrosis

In hydronephrosis, the renal artery is usually displaced upward by the dilated renal pelvis, and the intrarenal branches are markedly stretched. In the nephrographic phase, pronounced widening of the calyces, infundibula, and pelvis is seen. The degree of vascular opacification of the involved kidney is a reasonably good measure of the amount of functioning parenchyma. Abdominal aortography may also demonstrate an unusually located renal artery, or multiple renal arteries which may act to cause the hydronephrosis by compressing the ureter, pelvis or infundibulum.

4. Renal Malformations

Renal arteriography may be useful in demonstrating certain renal malformations, as previously listed.

5. Assessment of potential recovery of kidney function

It has recently been found that renal arteriography may be used to assess the potential recovery of function of a kidney that might be expected to occur after treatment of certain diseases, such as ureteric obstruction and chronic pyelonephritis. This is especially true in children. These diseases involve loss of functional renal parenchyma, which may be estimated on the nephrogram. More importantly, experiments have shown that the width of the renal artery parallels the loss of functional parenchyma. If the diameter of the renal artery is less than one half of normal, the loss of renal function may be considered irreversible. If the diameter is greater than one half of normal, some recovery of renal function may be expected to occur if the cause of the loss of functional parenchyma is removed. These findings have a therapeutic application. For example, in a case of ureteric obstruction caused by a ureteric stone, if the renal arterial diameter appears greater than one half of normal, removal of the stone may be carried out. With a renal arterial diameter less than half normal, nephrectomy might be advised.[1] The validity of this approach is controversial.

6. Pre-nephrectomy investigation

Aortography is a routine part of the investigation whenever nephrectomy is planned. Knowledge of the arterial supply in the diseased kidney is essential. The condition of the opposite kidney must also be assessed before removal of a diseased kidney. Aortography is also performed to assess the kidney of a prospective donor before transplantation. Radiographic evidence of kidney disease, or the demonstration of multiple renal arteries, are contraindications to use of the kidney as a donor.

III ADRENAL GLANDS

Diagnosis of adrenal hyperplasia and adrenal neoplasia

Abdominal aortography and selective renal arteriography can be used to visualize the adrenal glands. The adrenal glands are supplied by numerous small branches which arise most commonly from the inferior phrenic artery, aorta, and renal artery. Frequently branches from one of these arteries predominate. Commonly a diffuse "blush" of the entire gland is seen, caused by capillary opacification.

It is usually possible to differentiate between adrenal hyperplasia and adrenal tumour by the arteriographic appearance. In adrenal hyperplasia, the glands are enlarged, but they retain their triangular shape. Adrenal tumours tend to be rounded and pathologic vessels may be seen within them. These vessels are quite common in pheochromocytoma and the more malignant cortical tumours, because of their greater blood supply. At least two deaths have been reported in patients with pheochromocytoma following translumbar aortography. The cause of death was hypertensive crisis. Presumably injection of the medium into the tumour results in some form of irritation and release of catecholamines. When pheochromocytoma is suspected, therefore, the patient should be placed on slow intravenous drip throughout the procedure, and a supply of phentolamine (Regitine), an alpha-adrenergic blocking agent, should be on hand for immediate IV injection if the blood pressure should rise significantly.

The assessment of the adrenal function by aortography should be supplemented by clinical and laboratory studies, for in itself it may not always be diagnostic.

IV PANCREAS

Detection of space-occupying lesions of the pancreas.

Space-occupying lesions of the pancreas may be investigated by selective catheterization of the coeliac and/or superior mesenteric arteries. Two catheters may be used simultaneously, one in each artery. During the arterial phase, a peripancreatic arterial circle may be

seen, as well as abnormal intrapancreatic vessels. Visualization of the pancreatic parenchyma is frequently not good, even in the normal state, since this organ has a relatively meagre blood supply.

In expansive processes such as pancreatic cyst or carcinoma, the peripancreatic and intrapancreatic arteries will be displaced and stretched; they may also be invaded or occluded.

V GI TRACT

1. Determination of site of acute bleeding

Coeliac arteriography has been performed to locate unknown sites of acute bleeding from the gastro-intestinal tract. The site of bleeding becomes opacified only if the bleeding rate is high. This procedure has found little practical use.

2. Mesenteric arterial insufficiency

Arteriography of the superior or inferior mesenteric arteries is used for the diagnosis of mesenteric arterial stenosis or occlusion. Abdominal angina is the occurrence of periumbilical or generalized abdominal pain one to two hours after meals. The acute pain of mesenteric infarction may intervene at any time. Prompt diagnosis and removal or bypass of the obstruction are required.

3. Mesenteric cysts

Mesenteric cysts are uncommon. They may grow quite large, however, and cause intestinal obstruction. Mesenteric arteriography will show wide displacement and stretching of the arteries, typical of a non-vascular space-occupying lesion.

4. Mesenteric metastases

Mesenteric metastases may be recognized on arteriography as areas of increased radiodensity, with pathologic vessels. Arteriography of the mesenteric arteries is not useful in the diagnosis of primary tumours of the gastro-intestinal tract, except in the case of vascular tumours (hemangioma).

VI LIVER

Injection of medium into the coeliac artery may be used to visualize the hepatic arterial tree. Since as much as four-fifths of the blood supply of the liver comes from the portal venous system, portal venography is frequently more informative than arteriography in the presence of large, avascular space-occupying lesions. Vascular neoplasms, especially hepatomas, are best shown by the hepatic arteries.

The normal hepatic arteriogram is characterized by a very orderly branching of sharply defined vessels, running a smooth course to the periphery. The right hepatic artery and its branches are usually more easily seen than the left. Neoplastic areas in the liver may show increased vascularity and pathologic vessels. Quite fine branches may be seen to come directly from the large hepatic and gastroduodenal arteries. Areas of tumour involvement also exhibit early filling and late retention of the medium, as was described for the kidney. Focal areas of opacity may thus be seen when the rest of the liver is already relatively free of contrast material. The pattern just described applies to primary tumours or metastatic growths from such organs as the colon, stomach, pancreas, ovaries and lung.

A somewhat different pattern is seen in Hodgkin's disease of the liver. Because hepatomegaly is generally present, with the mass of the organ being increased relative to its blood supply, the vascularity of the liver may give the appearance of being decreased. The arteries are relatively more narrow in diameter; they appear to branch less frequently, and taper more quickly as they near the periphery.

Cysts of the liver typically have the appearance of a more vascular mass. The normal arteries about the cyst are displaced and stretched. The area of the cyst itself is poorly opacified, but this is difficult to recognize in small cysts.

SUMMARY

This article is a summary of the uses of abdominal angiography. The emphasis is upon the radiographic appearances of the more common abnormalities. Some basic radiographic principles, which apply to other areas of the body as well, e.g. the differentiation of a vascular and a non-vascular mass, pathologic vessel formation, and capillary opacification are described.

Reference is made to a few of the controversial aspects of this relatively new diagnostic tool.

The safety and usefulness of abdominal angiography is steadily increasing with continuing improvements in procedural technique and radiopaque media.

ACKNOWLEDGEMENTS

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REFERENCES

1. Golden, *Diagnostic Roentgenology*, Vol. 4, L. Robbins (ed.), Williams & Wilkins Co., 1968.
2. Abrams, H. L.: *Angiography,* Vol. I and II, Little, Brown & Co., 1961.
3. Allen, E.; Barker, N. and Hines, E.: *Peripheral Vascular Diseases,* Third ed., W. B. Saunders Co., 1962.
4. Holt, J. F.; Whitehouse, W. and Latourette, H.: *The Year Book of Radiology, 1967-1968 Series,* Year Book Medical Publishers Inc., 1968.
5. Holt, J. F.; Whitehouse, W. and Latourette, H.: *The Year Book of Radiology, 1969,* Year Book Medical Publishers Inc., 1969.
6. McLaren, J. W.: *Modern Trends in Diagnostic Radiology* (Third Series), Butterworth & Co. (Publishers) Ltd., 1960.
7. Sutton, D.: *Textbook of Radiology*, E. & S. Livingstone Ltd., 1969.
8. The Radiologic Clinics of North America, *Angiography in Retrospect and Prospect,* Vol. II, No. 3, W. B. Saunders Co., Dec. 1964.
9. The Surgical Clinics of North America, *Vascular Surgery,* Vol. 46, No. 4, W. B. Saunders Co., Aug. 1966.

Angiography In The Diagnosis Of Pulmonary Embolism

A. Abubakare, B.Sc., 7T0

INTRODUCTION

The incidence of pulmonary embolism has been reported to be 10% in routine autopsies. After pneumonia and emphysema, it is the third most common problem in pulmonary disease. Pulmonary embolism claims over 47,000 deaths annually in the United States and is a contributing factor in three times as many more deaths. Besides the recognition of the clinical manifestations, a high index of suspicion is required of both the clinician and the radiologist for an early diagnosis to be made. Deep venous thrombosis predisposes to embolic episodes and accounts for 95% of pulmonary emboli. Factors associated with deep venous thrombosis include surgical procedures, malignant disease, cardiac disease, leg injury, obesity, immobility, polycythemia, oral contraceptives and hypercoagulable states. Some increase in incidence in young healthy individuals has been reported; venostasis through prolonged sitting while watching television, or during air and automobile travel may be a contributing factor.

Although wide variations occur in mode of presentation, the common clinical symptoms and signs are dyspnea, pleuritic pain, hemoptysis, tachycardia, fever and phlebitis . Dyspnea is said to be the commonest symptom, occurring in about 64% of cases (Israel & Goldstein).

Pulmonary embolism may be classified into three types:

a. Micro-embolism — may be found typically in young females and characteristically produces pulmonary hypertension after several years.

b. Branch embolism — usually not fatal; frequently mis-diagnosed as pneumonia or a chest complication of myocardial infarction.

c. Massive embolism — often fatal and involving the main pulmonary arteries or proximal branches.

Often the plain chest roentgenograms do not give the required positive information needed to make a diagnosis. In embolism, the plain chest X-ray classically shows:

a. ischemia of the involved lung, peripheral to the site of the obstruction and appearing as a region of relative radiolucency.

b. dilated hilar arteries which will be more apparent if a previous chest film is available.

c. dilatation of the patent pulmonary arteries on the unaffected side.

d. pleural effusion.

e. elevation and fixation of diaphragm.

Figure 1: Pulmonary Angiogram of a normal adult.

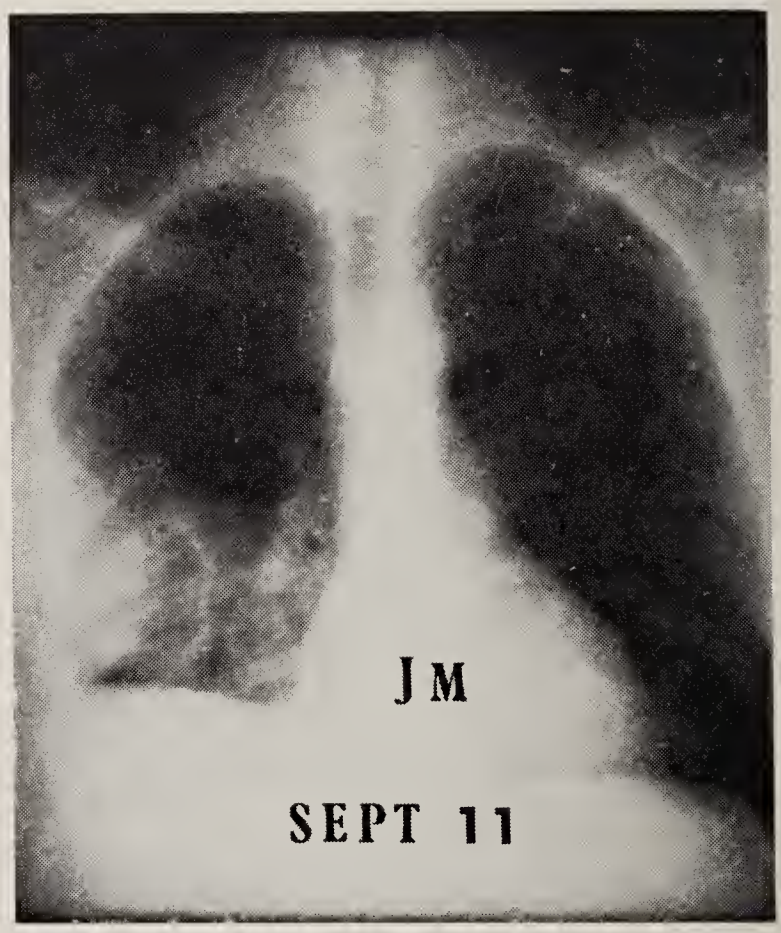

Figure 2. A fairly typical chest x-ray of a patient with proven embolism and infarction, showing a peripheral, wedge-shaped area of infarction in the right lower lobe, elevation of diaphragm, and pleural effusion.

With infarction, which occurs in less than 50% of pulmonary embolism, there are added signs:

f. segmental opacification which characteristically presents with its convexity pointing towards the hilum — the "Hampton's hump".

g. atelectatic plaques.

However, often supra- and infra-diaphragmatic causes may produce some of these signs.

The only two diagnostic procedures for this disease are radio-isotope scanning and angiography. Although the scan may in some cases rule out pulmonary embolism, it is less specific in demonstrating and differentiating between emboli with and without infarctions or excluding avascular areas due to atelectasis, air trapping, tumours, effusions, cysts and pneumonia. Angiography offers the best and most practical method of confirming the occurence, extent and location of an embolic process before decisive surgical therapy can be instituted. Its accuracy has been reported to be above 75%. It has been found helpful in identifying significant embolic disease in the contralateral lung of patients with unilateral symptoms, and usually demonstrates more extensive embolization than clinically suspected. Some reluctance towards the utilization of angiography in patients with suspected embolism exists; this is due, in part, to a fear of complications and to a fear of the procedure being too rigorous for routine use. A survey of several years ago placed the mortality from angiography at 0.38%. While morbidity cannot be ignored, it must be realized that a greater risk exists through temporizing or blind embolectomy. In the hands of the well-trained, a pulmonary angiogram can easily be done even on the severely handicapped patient. Shown below is a selective angiogram of a patient who developed dyspnea, tachycardia and hypotension eight days after a right pneumonectomy for an alveolar cell carcinoma of the lung. The procedure was well tolerated and demonstrates typical obstructive patterns. (Fig. 3)

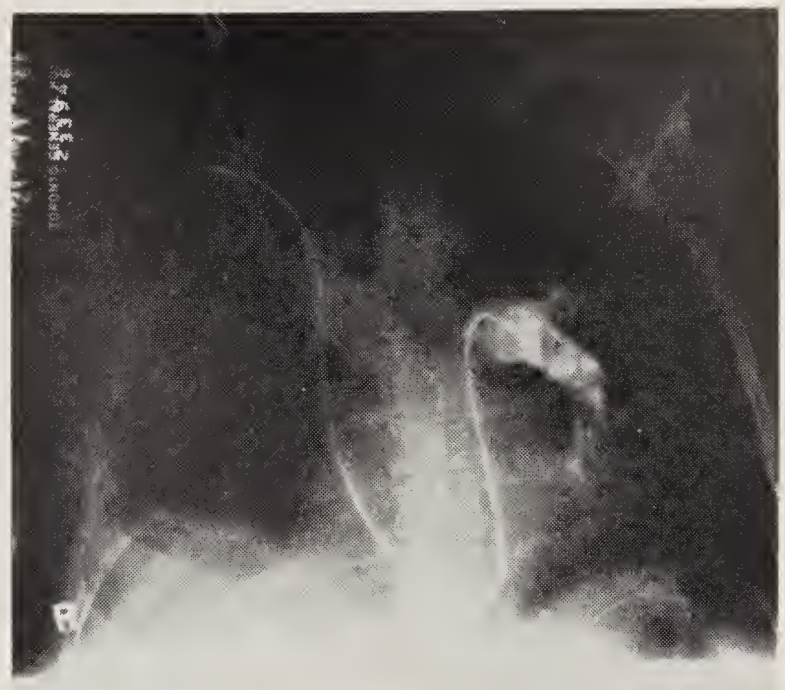

Figure 3: A selective left pulmonary angiogram, illustrating filling defects and the "pruned tree' appearance.

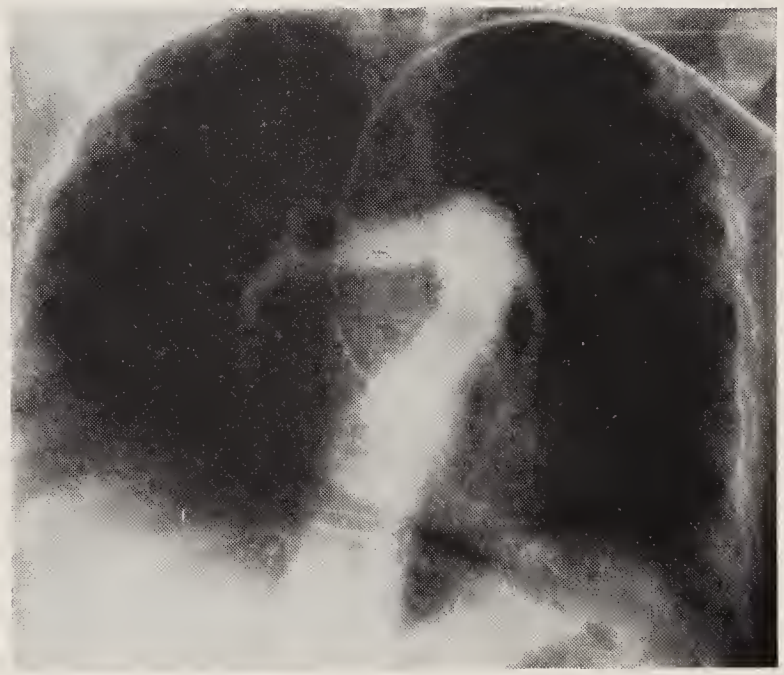

Figure 4: Pulmonary angiogram illustrating multiple filling defects (some arrowed), and hypovascularity in the regions of the right middle and left lower lobes.

METHOD

Two approaches are available:—

i. the peripheral route, that is, direct injection into the antecubital vein. This is probably the fastest and simplest method in the severely ill patient, but poor definition of the pulmonary arterial tree is obtained and hence, this method is rarely used.

ii. catheterization of the outflow tract of the right ventricle and/or pulmonary artery through the antecubital or femoral veins. This is the procedure of choice since it provides excellent demonstration of vascular details with good filling in both arterial and venous phases. Also, pulmonary artery pressures may be obtained or a selective pulmonary angiogram performed via this method.

INTERPRETATION

In the normal pulmonary angiogram:—

i. there is prompt and uniform opacification of the branches of the pulmonary arterial tree, the distribution of the lobar and segmental arteries corresponding to the divisions of the bronchial segments (Fig. 1).

ii. the arterial branches do not remain opacified nor is there evidence of retardation of flow.

iii. during the venous phase, pulmonary veins from all the lobes fill with contrast agent almost simultaneously, and drain into the left atrium at a level inferior to the main pulmonary artery. The segmental veins of the upper and middle lobes run parallel to and lateral to the pulmonary arteries. The lower lobe segmental veins pursue a more horizontal course, crossing the more vertically oriented arteries.

iv. the levophase of the angiogram shows opacification of the left side of the heart.

In embolic disease, changes due to anatomic alterations and pathophysiologic impairment are seen according to the duration, size, number and location.

i. Larger arteries and their segmental branches, when completely obstructed show an abrupt cut-off of the contrast-filled vessels, the margins normally being concave, squared-off or rarely convex forward.

ii. With incomplete obstruction a filling defect is seen, the configuration being lobular or wormy or conforming to the contour of the involved vessel.

When present these two signs constitute an angiographic diagnosis of embolism.

iii. The main pulmonary artery may be dilated.

iv. Arterial stasis resulting from complete obstruction of a larger vessel, trapping of contrast material around or within a clot, or micro-embolic obstruction to peripheral flow may be observed during the capillary and venous stages.

v. Occasionally, segmental avascularity and absent, diminished or retarded segmental venous return may be seen, depending on the size and number of the involved vessels as well as the available collateral circulation.

vi. Micro-emboli produce a pattern typified by plump arteries supplying the affected area, relatively sparse branches, or tortuous, shrunken and horizontal terminal branches diminished in number and appearing like a pruned tree (Figure 3). Micro-embolism is very hard to diagnose even by angiography but the use of the magnification technique may improve recognition of changes in the small peripheral vessels.

vii. Intracardiac defects and dilatation of the right cardiac chambers may be seen if contrast media is injected directly into these chambers. Phasic reflux of contrast media into the hepatic veins, due to tricuspid insufficiency or right inflow stasis with dilatation of the azygous vein, may be seen depending on the positioning of the catheter.

About 50% of patients who die of massive pulmonary embolism will have a history of previous embolism or venous thrombosis. It is therefore important that where embolism is suspected, angiographic assessment should be carried out, so that adequate treatment can be instituted.

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REFERENCES

1. Ferris, E. J.; Stanzler, R. M.; Rourke, J.A.; Blumenthal, J; Messer, J. V.: Pulmonary angiography in pulmonary embolic disease, Amer. J. Roent., 100:355-363, June, 1967.
2. Ferris, J. S.: The radiologic spectrum of pulmonary disease, Med. Clin. N. Amer., 53:375-383, March, 1969.
3. Fleischner, F. G.: Pulmonary embolism, Clin. Radiology, 13:169-182, 1962.
4. Israel, H. L.; Goldstein, F.: Varied clinical manifestations of pulmonary embolism, Ann. Int. Med., 47: 202-226, 1957.
5. Lowman, R. M.; Reardon, J.; Hipona, F. A., et al: The role of pulmonary angiography in pulmonary embolism, Angiology, 18:291-305, May, 1967.
6. Roberts, M.; Molnar, W.; Marable, S. A.; Wooley, C. F.: Angiography in recent pulmonary embolism, Radiology 87:713-715, Oct., 1966.
7. Robbins, S. L.: Pathology. Philadelphia, W. B. Saunders Co., 1967, pp. 705-707.
8. Sanders, D. E.: Pulmonary embolism, unpublished notes, Dec., 1968.
9. Sasahara, A. A.; Stein, M.; Simon, M.; Litman, D.: Pulmonary angiography in the diagnosis of thromboembolic disease, New Eng. J. Med., 270:1075-1081, 1964.
10. Schwaber, J. R.: Diagnosis of pulmonary embolism, Med. Clin. N. Amer., 53:365-373, Mar., 1969.
11. Wiener, S. N.; Edelstein, J.; Charms, B. L.: Observations in pulmonary embolism and the pulmonary angiogram, Amer. J. Roent., 98:859-873, Dec., 1966.

INDEX TO ADVERTISERS

C. C. Kilner Agency 95
Charles E. Frosst & Co. ..... Outside Back Cover
Homewood Sanitarium 91
Jobst Centre ..... 116 & Inside Back Cover
Ontario Cancer Institute 95

Hysterosalpingography

Sherryn Levinoff 7T0

INTRODUCTION

The advancement of radiology in diagnostic and therapeutic roles has reached every system of the body, including the female genital tract. Hysterosalpingography has allowed us to examine the anatomy of the uterine tubes and assess their patency, to assess the anatomy and outline of the uterus and its endometrial cavity, visualizing anomalies and pathological lesions, and also, to view the cervix and the endocervical canal.

INDICATIONS FOR HYSTEROSALPINGOGRAPHY

1. *Infertility*

The most common use for hysterosalpingography is in the investigation of infertility. Usually, a negative Rubin's Carbon Dioxide Insufflation Test has previously indicated blocked tubes, but hysterosalpingograms are superior in that they can indicate whether tubes are patent and functioning normally, and, if they are blocked, the exact location of the obstruction, especially important if surgical reconstruction is contemplated. In assessing the "peritoneal factor", i.e. whether there is normal function of the ovarian tubal transfer mechanism or whether the fimbriae appose the ovary or sweep the ovum from the cul-de-sac at ovulation without interference from intervening adhesions, hysterosalpingography has been somewhat helpful. These adhesions are usually secondary to disorders such as endometriosis, previous pelvic inflammatory disease, or prior appendicitis or peritonitis. Before concluding that tubes are not patent, a minimum of six insufflations and a hysterosalpingogram should be done, thereby providing a possible therapeutic effect in conjunction with establishing a diagnosis, since the slight pressure with which the dye is injected may force out mucous plugs or weak fibrous adhesions in the distal portion of the tube.

FIGURE 1—Normal hysterosalpingogram.

FIGURE 2—Blockage of both Fallopian tubes with no dye extending beyond the uterine cavity.

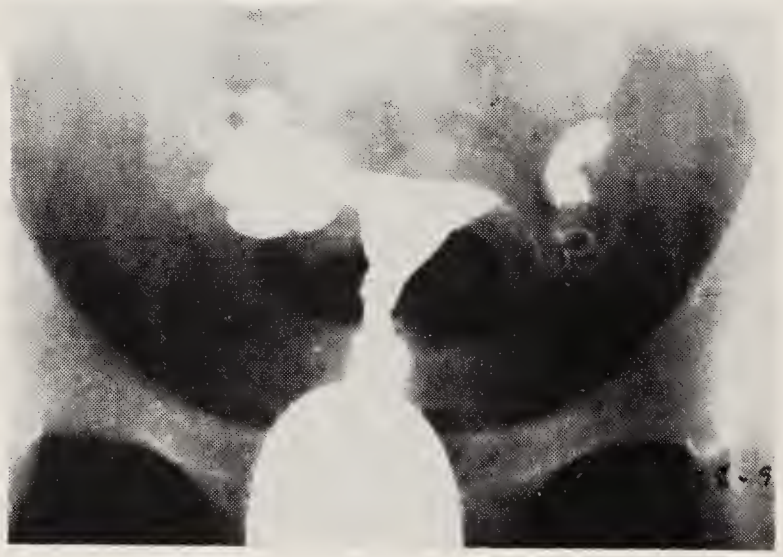

FIGURE 3—Bilateral tubo-ovarian masses indicating adhesions from previous pelvic inflammatory disease.

There is often spasm of the cornual end of the fallopian tubes which simulates pathological occlusion. This is due to the introduction of a foreign body, either cannula or contrast media, which the uterus attempts to expel by contraction. To overcome this, patients can inhale amyl nitrite at the time of insufflation or hysterosalpingography or be given intramuscularly 10 mg. isoxsuprine hydrochloride (Vasodilan*) one half hour before the procedure. Vasodilan is a myovascular relaxant which acts directly on smooth muscle of blood vessels and uterus with low toxicity and good tolerance, producing an antispasmodic and relaxant effect on uterine muscle.

Also, in patients complaining of infertility, abnormalities of the uterine cavity may be discerned e.g. bicornuate uterus, submucous fibroids, large polyps, and neoplasms. Coincidentally and rarely, a diagnosis of carcinoma of the fallopian tubes may be made.

In patients who have been habitual aborters this technique can often confirm a tentative diagnosis of

incompetent cervical os. For this, a special balloon catheter is placed in the endocervical canal and lower fundus. The catheter is inflated with aqueous contrast dye and shows clearly the outline of the cervical canal and internal os.

2. *Menstrual Abnormalities*

Primary and secondary amenorrhea may be investigated by hysterosalpingograms. The diagnosis of Asherman's syndrome i.e. synechiae (adhesions) of the anterior and posterior walls of the uterus following curettage associated with severe endometritis can be confirmed. Hypoplastic or non-existent uterus can also be revealed.

3. *Abnormal Gestations*

Patients with abnormal pregnancies can be investigated by hysterosalpingography; however, it is dangerous and not recommended. The diagnosis of ectopic tubal pregnancy can be made, but injected fluid may rupture the tube or increase the bleeding. The diagnosis of hydatidiform mole can also be confirmed, but dye must not be injected in the conventional manner via the cervical route, since this may introduce infection or rupture the membranes of a normal pregnancy. Rather, 10 to 60 ml. of a 25% Sodium Diatrizoate solution is introduced transabdominally into the uterus. If a mole is present, radiolucent areas of different sizes (5 to 15 mm. in diameter) surrounded by shadows of greater density will be seen. If at any time amniotic fluid, denoting a normal intrauterine pregnancy, is extracted, the procedure is terminated. This is not called amniotomy since there is not a true amniotic cavity with a molar pregnancy. Using the above method, investigators have been able to distinguish between hydatidiform mole, chorioadenoma destruens, and choriocarcinoma. There are very few failures with this technique and the diagnosis can be made early and immediately.

4. *Assessment of Uterine Scars*

Hysterosalpingography can be used to assess the strength of a uterine scar following Cesarian Section in the non-pregnant state; however, this does not necessarily test the integrity of the scar under the stress of labour.

5. *Location of IUD*

By using double contrast hysterosalpingography, one can assess the position of an intrauterine contraceptive device and deduce its relationship to pain and metrorrhagia and the amount of uterine cavity protected by the device. If the dye is merely injected into the uterus, the IUD will be hidden by the contrast media. Therefore, after the contrast media has reached the cornua (seen on the image intensifier screen), carbon dioxide is injected under light pressure until the uterine cavity is almost evacuated of dye. Then one exposure is taken showing the outline of the IUD, uterine cavity, and tubes. If the same position of the patient can be retained for two films, almost as good results can be obtained by taking a plain film of the abdomen with the IUD in place and then a conventional hysterosalpingogram, and subsequently superimposing them.

PROCEDURE

The hysterosalpingogram is best done between days nine to fifteen of the menstrual cycle. The patient is placed in lithotomy position on a special table similar to that used for cystoscopy or pyelography. A speculum is introduced to expose the cervix and a tenaculum applied to the anterior lip. The cervical os is swabbed with Schiller's solution as an antiseptic. A uterine sound is inserted to discern the depth and direction of the cervical canal and to gently dilate the cervical canal and internal os. A special cannula, made of nylon or metal with a rubber stopper to produce a tight seal, is introduced into the cervix. The outer end of the cannula has a Luer-Lock syringe attachment to allow injection of contrast media. The tenaculum is locked onto the cannula anteriorly so as to apply countertraction and to keep the seal airtight at the cervix. Before insertion into the cervical canal, the entire system should be filled with radiopaque dye to avoid injection of air bubbles which will later create artefacts resembling uteral or tubal disease, such as uterine polyps.

FIGURE 4—Normal pattern of dye spillage into the abdomen after hysterosalpingography, indicating Fallopian tube patency.

A scout film of the abdomen is usually taken first to determine prior presence of radiopaque substances in the body. Then slowly, 1 to 2 cc. dye are injected, to

outline the uterine cavity and clearly view any abnormalities, e.g., submucous fibroids, polyps, etc. Another film is then taken, while watching for sensitivity of the patient to the dye. At this point, a further 2 to 4 cc. is injected under light pressure to determine patency of tubes if not already disclosed from the first film. A second film is taken after which, if negative, the patient can be rotated to the left and right successively to aid in spillage of the dye. Depending on whether oily or water-soluble contrast media is used and if results are still questionable, other films may be taken later at 2 and 24 hours seeking dye in the peritoneal cavity.

There are various contrast media available today. Originally iodized oil was used, but with the hazards of severe local reactions in the uterus and of pulmonary oil embolism, better dyes were sought. In attempts to devise a water-soluble dye, one encountered the difficulty of poor radiopacity, and any added ingredients also increased the viscosity. The dyes used today are chiefly Salpix and Sinagrafin (40% meglumine diatrizoate and 20% meglumine iodipamide), water-soluble with no added components but creating excellent contrast, even superior to oil, and causing little or no pain and muscle cramps.

Under the above conventional system, there are three or four exposures of the abdomen to radiation. Fluoroscopy has been generally contraindicated, since it involves unnecessary excess use of radiation to both the patient and the physician. However, this idea has been criticized since with the image intensifier and television control, the procedure can be done in less time, using less dye, with less discomfort to the patient and with a better evaluation of uterine and tubal motility and anatomy. If there is unsuspected endometrial pathology or poor timing between menses, the pelvic veins may be flooded with dye, whereafter the procedure should be discontinued. With fluoroscopy, it can be seen immediately that an insufficient amount of dye has been injected into a large uterine cavity and the tubes subsequently not filled or that there is unilateral differential filling of the tubes due to spasm or tortuosity on the contralateral side, flooding the pelvis. This defect can be corrected instead of requiring further injections. The positioning of the uterine cavity is also important. If it is not directly an 'en face' view, poor visualization will result, and at least one exposure will be wasted.

CONTRAINDICATIONS

1. *Bleeding*

Any active uterine bleeding, fluid or clotted blood will produce artefacts or mask pathology and uterine sinuses will pick up the dye into the vascular system.

2. *Infection*

In the presence of any genital tract infection, peritonitis or gram negative septicaemia may follow this procedure. Wait at least four to six months after an episode of pelvic inflammatory disease before attempting hysterosalpingography.

3. *Pregnancy*

Unless, as stated above, a mole is suspected and the transabdominal route is employed, pregnancy strongly contraindicates this procedure.

4. *Curettage*

After curettage of a patient, a four to six months waiting period is recommended before hysterosalpingography.

COMPLICATIONS

1. *Mechanical*

Without any genital tract pathology, the patient may experience lower abdominal pain related to instrumentation, the type of dye instilled, and the injection of the contrast media. However, with an overdistended uterus and with instillation of dye into blocked tubes, the patient will have significantly greater pain. The pain will become much more intense if the pressure has ruptured a tubal pregnancy or pyosalpinx, and tenderness will also be evident in the subcostal spaces and shoulder tips.

The instrumention, i.e. sounding the uterus before the procedure or the introduction of a cannula with a tip protruding more than 1 cm. beyond the rubber stopper, can cause laceration or perforation to the genital tract. Theoretically, endometriosis can also be caused, since there is reflux of viable endometrial tissue into the cul-de-sac and onto the ovaries. However, no definite case of this complication has been proved. Hemorrhage may occur from either the site of application of the tenaculum or from an organic irritated lesion.

2. *Chemical and Toxic*

The contrast media may cause an aseptic inflammatory reaction in the mucous membranes resulting in granuloma formation. No one dye has been incriminated specifically although carboxymethyl cellulose was removed from the list of available media. These granulomas can convert a once patent tube into a blocked tube although this rarely happens with absolutely normal tubes, since active peristalsis will not allow dye to be retained.

Cases of sensitivity with urticarial reactions have been reported with the iodine and iodized oil. Iodine dyes, especially the oily ones, will change the results in thyroid function tests, overestimating PBI values and underestimating thyroid I^{131} uptake. Therefore, any thyroid testing should be done before hysterosalpingography.

3. *Radiation Hazards*

There is a potential somatic as well as a genetic danger, i.e., both to the radiated person herself and to

her progeny. The radiation effect is cumulative, increasing the possibility of cell mutation. No procedure should be done unnecessarily, hence, this danger is another reason to do carbon dioxide insufflation tests first.

4. *Intravasation*

Contrast media may spill into the uterine musculature, blood vessels, and lymphatics. This occurs in approximately 1% of patients. Direct trauma, excessively high pressure or deficient endometrium can all be the cause of dye entering the uterovenous sinuses. If the intravasation continues, pulmonary embolism, infarct, or severe pain may follow.

The entry of dye into the lymphatic system throws a cloudy, coarsely granulated shadow over the uterus, from wall to serosa. This finding is often associated with tuberculosis.

SUMMARY

Hysterosalpingography has proven to be an excellent and simple diagnostic aid on an out-patient basis, sometimes eliminating further investigation for tubal patency, e.g., culdoscopy or laparoscopy. There are very few adverse effects. Some common causes of infertility can be localized and treated more effectively, causes of menstrual abnormalities discovered, and life-endangering disease detected earlier. The procedure is an excellent adjunct to the usual tools for investigating clinical problems, broadening knowledge in both obstetrical and gynecological fields.

REFERENCES

1. Altenus, R.; Charles, D.; and Yoder, V.: Conventional Hysterosalpingography Used in the Evaluation of Sterility Problems, A Critical Analysis, Fertil. Steril. 18:713-8 Sept.-Oct. 1967.
2. Behrman, S. J. and Gosling, J. R. G.: Fundamentals of Gynecology. New York: Oxford University Press (1960).
3. Fischer-Rasmusser and Guttorm, E.: Double Contrast Hysterosalpingography for the Visualization of Intrauterine Contraceptive Devices, Acta Obstet. Gynec. Scand. 46:92-8, 1967.
4. Page, E. P.: Use of Isoxsuprine in Uterosalpingography and Uterotubal Insufflation, Amer. J. Obstet. Gynec. 101:358-64, 1 June 1968.
5. Roland, M.; Clyman, M.; and Decker, A.: Further Studies on the Value of Water-Soluble Media in Hysterosalpingography, Fertil. Steril. 17:605-12, Sept.-Oct. 1966.
6. Senties, L.; Perdoma, A.; and Luna, R.: Diagnosis of Hydatidiform Mole by Hysterography through Transabdominal Injection, Obstet. Gynec. 33:352-7 March 1969.
7. Siegler, A.M.: Dangers of Hysterosalpingography, Obstet. and Gynec. Survey 22:2:284-308 April 1967.

Symptomatology — *Tetany*

Tetany is a manifestation of increased neuromuscular irritability. It is marked by intermittent tonic muscular contractions, fibrillary tremors, paresthesia, and muscular pains. Clinically, two forms are distinguishable: that related primarily to hypocalcemia, and that related primarily to alkalosis.

CLINICAL MANIFESTATIONS

A. Latent Tetany

In this phase of tetany, mechanical or electrical stimuli are required to elicit signs of the increased muscular excitability. The following are some of the classical manoeuvres carried out.

i) *Chvostek's Sign* – Taping over the facial nerve elicits an ipsilateral contraction of the facial muscles around the mouth, nose and eye. Although this sign may be present in normal individuals, one should suspect tetany in any child between three months and three years (the vitamin D deficient age range) who gives a positive sign.

ii) *Peroneal Sign* – In this case, tapping over the personal nerve just distal to the head of the fibula will cause dorsiflexion and abduction of the foot. The knee should be slightly flexed during this test.

iii) *Trousseau's Sign* – Inflation of the sphygomomanometer cuff on the arm to more than systolic blood pressure is followed by a characteristic spasm of the forearm and hand. The wrist is flexed, the fingers are flexed at the MP joints, extended at the PIP and DIP joints, and the thumb is abducted into the palm. This position is referred to as "accoucheur's hand".

iv) *Erb's Sign* – Of historical interest, this sign measures the amount of galvanic current required to produce muscular contraction. It is perhaps the most sensitive of the tests for muscular irritability.

B. Manifest Tetany

During this stage, the symptoms of hyperexcitability are clearly evident and may include convulsions, spontaneous twitching and laryngospasm.

i) *Carpopedal Spasm* – The hands are in the position described above under Trousseau's sign. Also, the foot assumes an equinovarus posture with the toes flexed and the sole cupped. The arms and legs may be rigidly flexed and abducted.

ii) *Laryngospasm* – In paediatric tetany, spasm of the muscles of the glottis is not common, and may produce an inspiratory, high-pitched crowing sound. If severe enough, the spasm may lead to respriatory distress with cyanosis.

iii) *Convulsions* – These appear as generalized seizures. However, carpopedal spasm only, may be present.

(Continued on page 112)

Radiation In Therapy

May Ho 7T1

INTRODUCTION

The use of ionizing radiation for therapeutic purposes dates back to the turn of the century, soon after the discovery of Roentgen rays in 1895. Through the years, knowledge of the effects of radiation has accumulated from clinical and laboratory observations. Nevertheless, even today, the basic mechanisms of cellular effects of radiation have not been fully elucidated. In this paper, an attempt will be made to review the basics of radiation biology and its clinical application, with the hope of stimulating further reading in this comparatively new and very exciting specialty.

RADIATION EFFECTS ON THE CELL

When ionizing radiation is passed through living matter, high energy particles knock off electrons from some of the atoms in the cell. These excited and ionized atoms are intensely reactive and they instantaneously enter into some new chemical combination in their immediate environment, altering the chemical composition of the material they react with. The process has no significance when the material affected is not vital to the survival of the cell, or when it can be replaced by synthesis within the cell. Radiation damage at the cellular level occurs mainly when the DNA is affected. The following steps are involved:

(1) Scission of DNA followed by enzymatic degradation, with some DNA moiety being more susceptible than others.

(2) Halting of genetic transcription, with possible subsequent recovery.

(3) Reduction of rate of synthesis.

(4) Repair processes which are effective to different extents at different stages in the cell cycle.

These alterations are not apparent during interphase, but as the cell enters mitosis, a number of defects may be observed. The chromosomes are changed in form, being broken up or joined together in abnormal ways. There may be spindle abnormalities, e.g. three instead of two poles. Chromatids tend to stick together at anaphase resulting in uneven distribution of the genetic material within daughter cells. Sometimes, giant cells are formed when chromosomes divide independently of the cell or when the nucleus divides independently of the cell.

Besides acting on cellular DNA, radiation has also been observed to induce other biochemical changes in the cell.

(a) Inhibition of oxidative phosphorylation — Mitochondria from the spleens of rats given 800r whole-body irradiation showed a decreased capacity to carry out oxidative phosphorylation.[1] The mechanism is believed to be either a direct effect of radiation on the enzyme system or an indirect one due to mobilization of an endogenous inhibitor e.g. thyroid hormone.

(b) Inhibition of nuclear ATP synthesis — This effect occurs readily. Since nuclear ATP is not essential to cell survival, its importance in radiation injury is doubtful.

(c) Inhibition of RNA – The effect on RNA synthesis may be secondary to radiation injury to DNA. The alteration of a DNA molecule necessary for the synthesis of a messenger RNA for a vital protein can lead to serious consequences.

(d) Structural and functional alterations in proteins – This action tends to localize at sulfhydryl and disulphide groups. Of particular importance are the histones which are believed to regulate the rate of DNA and RNA synthesis.

(e) Cellular disorganization – The disruptive changes include dilatation of vesicles, swelling of mitochondria, and rupture of the plasma membrane. Radiation also increases cellular permeability by its effect on the sodium pump, thus altering the internal environment of the cell.

(f) Release of enzymes from lysosomes – This may be sufficient to cause cell death.

CLINICAL APPLICATION

Irradiation in the treatment of malignancies is based on the selective destruction of neoplastic cells which are more vulnerable than their normal counterparts by virtue of their greater rate of cell division. There exists a difference in radiosensitivity between normal and neoplastic tissues, which is defined as the relative change towards a given end point (usually decreased tumour size or altered function) produced in a cell, an organ or an individual by a given dose-time-volume relationship.

Several factors contribute to the degree of radiosensitivity of a particular tumour. Radiosensitivity is influenced by the behaviour of the cell during exposure. Cells about to divide are more sensitive than so-called resting cells. The origin of the cell is also important. In undergoing malignant transformation, cells invariably increase in radiosensitivity, but the magnitude of this change depends on the type of cell concerned. Of even greater importance is the oxygenation of the tumour tissue. Increased dissolved oxygen, in general, increases sensitivity. Such a principle has been applied to treatment of advanced gliomata, mouth and cervical tumours

by the use of hyperbaric oxygen. Unfortunately, at least one retrospective study showed that the method added little effectiveness[2].

Related to the degree of oxygenation in the tumour tissue is the problem of previous irradiation which appears to render the surviving neoplastic cells much more resistant. This could be caused by a radiation-induced mutation to a more resistant cell type. More likely it is due to a change in the tumour bed brought about by post-radiation fibrosis. The proliferation of subendothelial connective tissue narrows the blood vessels and hence reduces the oxygen supply to the surrounding tissue.

Radiosensitivity is not synonymous with radiocurability. To evaluate a patient for therapy, 3 other factors need to be considered:

(i) type of tumour – In general, squamous cell carcinoma is more sensitive than adenocarcinoma and adenocarcinoma is more sensitive than connective tissue sarcoma. However, there is wide variation within each cell type.

(ii) site and size of tumour – An accessible and localized lesion, even if it comprises a large part of the organ or area of origin, may be curable. In contrast, an easily accessible squamous cell carcinoma of the vulva would prove to be difficult to cure by irradiation, since vulvar tissue does not tolerate cancerocidal irradiation well. Radiotherapy is also unsuitable for treatment of carcinomatosis or diffuse lymph gland involvement since irradiation of a large part of the body results in appreciable morbidity.

(iii) general condition of the patient – In debilitated individuals, normal tissue tolerance is decreased and wound healing is slowed. With further deterioration of health, delayed radiation necrosis may occur. One should attempt to correct as many deficiencies as possible before starting treatment. Specific antibiotic medications, transfusions and general supportive care, if given early and adequately, increase the patient's chances of responding favourably to radiation therapy.

The effect of anaemia on the survival of patients treated for carcinoma of the cervix was reviewed recently[3]. The evidence points to the fact that patients with low haemoglobin at the onset of treatment show a lower survival rate than those with near normal hemoglobin.

All the information on which to base one's evaluation is available from a good history, complete physical examination, X-ray films, laboratory results, pathology from tissue biopsies and report from a surgeon who may have operated on the patient or performed specialized studies of any type, e.g. bronchoscopy.

In determining the dose of radiation, the "standard" for a given kind of tumour has been arrived at through years of clinical experience. However, each patient must still be evaluated according to his needs and tolerances. Furthermore, the period of time over which a certain dose is given is of vital importance.

When a given dose of radiation is divided over a period of time, the biological effect is usually less than if it had been given in a single dose. This decreased response with fractionation of the dose appears to be related to cell recovery as well as to the capability of cells not lethally damaged to adapt to radiation-induced alterations of the surrounding tissues. On the other hand, fractionation greatly reduces the damage to the adjacent normal tissues. Cater and Silver[4] also found that tumour oxygen tensions increase during or following irradiation while changes in normal tissues are slight or absent. This means that each fraction of the dose renders the next more effective by increasing the oxygenation. However, if daily fractions are too small, sterilization is impossible regardless of the total dose. Ideally then, what should be sought is a minimal daily dose and a maximal total dose that can be tolerated by the patient.

Once the three-dimensional region to be irradiated is established and a tentative dose decided upon, field arrangement and beam directioning are necessary. The utilization of a number of converging beams from different fields makes it possible to obtain the maximum dose in the area where all the beams are concentrated without subjecting the surrounding normal tissues to more than a fraction of the total tumour dose.

METHODS OF TREATMENT

The methods employed in radiotherapy can be divided broadly into those which utilize an *external source of radiation energy* and those in which the *source is implanted into the tissues* to be treated.

A. External Irradiation

1. *Deep X-ray Therapy* – X-rays have no mass or charge, and vary in their penetrability depending on the energy at which they are generated. The voltage of the machines now in use ranges from 200 to 2,000 kilovolts. The portion of the X-rays that are absorbed in the tissue brings about retrogressive changes in the component cells.

2. *^{60}Co Beam Therapy* – provides higher energy radiation than deep x-ray therapy does. It emits gamma rays essentially equivalent to the radiation of a 3,000,000 volt X-ray machine. As the maximum effect is focused on a plane 0.5 cm below the surface of the skin, there is much less skin reaction. However, this creates the problem that in the absence of visible skin changes it is possible to have serious future complications without any warning.

B. Internal Irradiation

1. *Intracavitary* – The basic system consists of a linear source of radiation in the long axis of the cavity,

which provides for the intensely concentrated irradiation of a limited field. Radium is most commonly used as the source. As it decays into its daughter elements, alpha and beta particles are filtered out by enclosing the radium in a glass tube which is in turn encased in a platinum tube, while the gamma rays are allowed to penetrate the surrounding tissues. The intensity of radiation around the source of radium falls off rapidly according to the inverse square law. The radium is removed after time is allowed for the delivery of a desired dose. This may be followed by one or two more insertions at intervals of approximately one week.

^{137}Cs and ^{60}Co may be substituted as sources of radiation energy.

2. *Interstitial* – This involves the use of radioactive needles which are implanted in radial or stockade fashion around the tumour. The needles are removed after delivering the desired dose. One special application of this method is the use of Yttrium^{90} pellets via the transnasosphenoid route for pituitary ablation.

3. *Radioactive Colloidal Gold* – ^{198}Au has a half life of 60 hours, and in the process of decay emits beta particles and some gamma rays. The former are responsible for most of the biological effect. Radioactive colloidal gold is used in serous cavities where it adheres to the serosal surface and penetrates to a depth of about 1 mm. It is useful in suppressing fluid formation resulting from neoplastic involvement of the serosal surface.

RADIATION EFFECTS

Superficially, there is at first erythema in the treated area, followed by desquamation and re-epithelialization of the skin in a few weeks with some increase in pigmentation, a little atrophy and telangiectasia.

In more severe cases, there may be vesicle formation, maceration and finally necrosis. However, this too will heal with growth of new epithelium coming in from the outer margins of the affected area.

Subcutaneously, fibrosis of the underlying soft tissues can have serious consequences. In the author's own limited experience with the Ontario Cancer Foundation clinic at Ottawa Civic Hospital one summer, some breast cancer patients treated with ^{60}Co beam therapy with a tumour dose of approximately 4000 Rads to the anterior chest wall and supraclavicular area have been observed in follow-up examinations to have considerable impairment of the function of the upper limb. There is exaggeration of the lymphoedema already present from the wide node resection in mastectomies, limitation of movement at the shoulder joint, pain and tenderness, brachial plexus damage as manifested by numbness, tingling and loss of motor function of the arm and hand, bony changes in the humerus and bones of the shoulder girdle, and very rarely, necrosis of the soft tissues in the chest wall and axilla.

In the abdomen, post-radiation fibrosis may lead to adhesion and obstruction of the bowels.

In spite of extensive shielding techniques, radiation occasionally affects the surrounding structures. This may produce castration in the treatment of carcinoma of the uterus, vesicovaginal and rectovaginal fistulae in the treatment of cancer of the cervix, and fracture of ribs in the treatment of breast cancer.

Systemically, nausea and vomiting are experienced with irritation of the small bowel, and rectal mucosal irritation leads to diarrhoea. These reactions may be severe enough to warrant a decrease in the daily dosage or the cessation of treatment altogether. However, the administration of antiemetic drugs and paregoric is often sufficient to bring about relief.

Finally, bone marrow is sensitive to irradiation. Depression of function with leukopenia and anaemia can result; however, even with high therapeutic doses, this is no more than a transient effect, and the marrow recovers full function with the end of irradiation.

POST-TREATMENT CARE

Follow-up examinations constitute an essential part of radiotherapy. The things to look for are the radiation effects cited above, signs of recurrence and distant metastases.

Initially patients are seen once every month for six months, then in 3 or 4 months, then in 6 months and finally annually.

RADIOTHERAPY AND SURGERY

Radiotherapy and surgery are often combined in a variety of ways in the management of malignancies.

A. Both modalities of therapy applied to different portions of the tumour complex.

(i) Primary tumour treated by radical irradiation, lymph node metastases by surgery. Treatment of the primary site should always precede surgery. This allows the tumour bed to be undisturbed during radiation. Surgery is carried out when one can evaluate the probability of control of the primary. The time required between procedures is the time necessary for the acute radiation reactions to subside, usually 3-6 weeks.

Some tumours of the head and neck, especially lesions of the skin and lip and well-differentiated squamous cell carcinoma of the upper respiratory tract appear to respond most favourably to this approach.

(ii) Primary tumour treated by surgery, lymph node metastases by irradiation. Surgery precedes irradiation in this case since in many conditions in this group, resection of the primary tumour is necessary for pathological diagnosis. Treatment should be initiated as soon as the surgical incisions are healed.

The main indications are testicular tumours, early cases of Wilm's tumour and neuroblastoma, and supraclavicular and internal mammary node metastases from a carcinoma of the breast.

B. Both modalities applied to the whole tumour complex (primary plus regional metastases).

(i) *Pre-operative irradiation* – This form of treatment is indicated for a primary cancer of unidentified boundaries. The cells at the periphery of a tumour are more radiosensitive than those in the core. If radiation is applied to an area greater than the anticipated area of surgical excision, it can control the cell nests and small lymphatic metastases neglected otherwise. Preoperative radiation also helps to prevent spillage of malignant cells into the operative field and the shedding of malignant cells into the circulation.

(ii) *Post-operative irradiation* – This is a prophylactic measure to control gross or microscopic residual disease at the margin of the resection and/or to destroy cells seeded in the operative field during surgical manipulation. The whole operative field must be irradiated, using the lethal dose.

REFERENCES

1. Potter, R. L.; Bethel, F. H.: Fed. Proceedings, 11:270, 1952.
2. Watson, T. A.; Banerjee, P.: J. of the Canadian Ass. of Radiologists, Vol. XX, June 1969.
3. Hierlihy, P.; Jenkin, R. D. T.; Stryker, J. A.: Canad. Med. Ass. J. June 21, 1969, vol. 100.
4. Cater, D. B.; Silver, I. A.: Acta radiol. 53:233-256, 1960.
5. Behrman, S. J.; Gosling, J. R. G.: Fundamentals of Gynaecology, 2nd edition, Oxford University Press, Inc., New York, 1967.
6. Fletcher, G. H.: Textbook of Radiotherapy, Lea & Fletcher, Philadelphia, 1966.
7. Murphy, W. T.: Radiation Therapy, 2nd edition, W. B. Saunders Co., Philadelphia and London, 1967.
8. Moss, W.: Therapeutic Radiology, 2nd edition, C. V. Mosby Co., St. Louis, 1965.
9. Schwartz, E. E.: The Biological Basis of Radiation Therapy, Lippincott, Philadelphia and Toronto, 1966.

TETANY (Continued from page 108)

The diagnosis of tetany is based then on
1) clinical examination
2) laboratory data: serum calcium in hypocalcemic tetany pH and electrolytes of blood in alkalotic tetany.

PATHOGENESIS

By increasing the concentrations of sodium and potassium ions, or decreasing the concentrations of calcium, magnesium and hygrogen ions, the irritability of muscle may be increased. The homeostatic mechanisms involved in maintaining normal relationships of these ions are the following:

i) resorption and formation of bone
ii) excretion of calcium and phosphate
iii) gastrointestinal absorption of calcium
iv) internal distribution of calcium and phosphate
v) intra and extracellular distribution of sodium, potassium, and hydrogen.

Hypocalcemic tetany usually manifests itself when the serum calcium is less than 7-7.5 mgm/100 ml. Often the newborn presents with tetany. It is postulated here, that the parathyroid glands respond inadequately to maintain calcium homeostasis. Neonatal tetany has also been related to maternal hyperparathyroidism, and/or over consumption of cow's milk. The latter contains a rather high phosphorus level, which, if absorbed excessively, inversely decreases calcium levels. Later in infancy vitamin D deficiency and celiac disease are the commonest causes of hypocalcemia and tetany.

Alkalotic tetany may be related to hyperventilation, where there is a great loss of plasma carbonic acid and small loss of bicarbonate. This respiratory alkalosis alters the proportion of ionized calcium, though the total content remains unchanged, thus producing tetany. Hysteria is a frequent cause of respiratory alkalosis because of its associated hyperventilation.

Recurrent vomiting, with its concomitant loss of chloride ion will cause an increase in plasma bicarbonate, with resultant metabolic alkalosis.

Overingestion or excessive intravenous administration of sodium bicarbonate, especially in patients with vomiting or chronic renal disease may also produce an alkalotic tetany.

It is also possible to cause hypocalcemia in an exchange transfusion, if calcium has not been given during the procedure.

CONCLUSION

Tetany then is a manifestation of neuromuscular irritability due to an underlying biochemical imbalance. With the aid of simple laboratory determinations such as Serum Ca, Serum pH and pCO_2 the underlying mechanism can be defined.

Barry W. Malcolm 7T1

Clinicopathological Conference

A Rapidly Growing Left Upper Quadrant Mass In An 18-year Old Male

CASE PRESENTATION

An 18-year-old boy was admitted to NMSH on August 18th, 1967, because he had noticed a mass in his left upper quadrant which had persisted and enlarged over the previous three months.

Functional enquiry revealed that the patient had indigestion and heartburn intermittently for several years, after eating greasy foods, and that this was now increasing in frequency. This was relieved by antacids. Two years previously he had an upper GI series done, which was negative, and was told that he had a "nervous stomach". His appetite had been poor, but he had no weight loss until that time. There was no history of fever or chills. He had two episodes of abdominal pain associated with vomiting; there was no history of hematemesis, or melena. The patient did not smoke or drink alcoholic beverages. There was no family history of cancer. In general the patient felt quite healthy, but noticed that he tired more easily, and was not as active as usual.

On physical examination, the patient appeared healthy, somewhat thin, and in no apparent distress. The only pertinent findings were in the abdomen. There was an area of fullness in the left upper quadrant. A large, hard mass, about 15 cm in diameter, was felt protruding from below the left costal margin. It lay superficially just beneath the anterior abdominal wall and extended deeply into the abdomen. It was not possible to get above the mass where it disappeared beneath the costal margin. The mass was smooth-surfaced, nontender, and descended mediallly towards the umbilicus on deep inspiration. There were no bruits or pulsations. Liver and kidneys were not palpable. Rectal examination was negative.

Laboratory findings at that time included the following: Urinalysis: S. G. 1.020, 2+ albuminuria, sugar 0, WBC 12-13, RBC 3-4, epithelial cells moderate, some hyaline and granular casts; Hematology: hemoglobin 12.6 gm %, WBC 8700; Blood Chemistry: total protein 6.8 gm %, albumin 4.6 gm %, globulin 2.2 gm %; Kahn tests non-reactive.

Extensive radiological investigation was carried out and revealed the following:

Chest X-ray: normal.

Plain film of abdomen: Showed a large, ill-defined, homogeneous density occupying the left upper quadrant of the abdomen, through which the left kidney and psoas shadows were clearly distinguishable. The outline of the spleen could not be well demonstrated. An amorphous calcification below and somewhat lateral to the tip of the left kidney may possibly have been within the suspected mass.

Intravenous pyelogram: There was prompt excretion and satisfactory concentration bilaterally. The collecting systems appeared normal. The left ureter was displaced medially by what appeared to be the above-mentioned mass. No obstruction or other abnormality was noted (Fig. 1).

Upper G.I. Tract: Oesophagus was normal. The stomach was fairly large and displaced to the left and anteriorly by the mass, with nodular indentation on the postero-lateral aspect of the stomach and with some stretching of the mucosal pattern, but with no intrinsic involvement of the mucosa itself. No other abnormality was noted in the stomach, duodenum, or small bowel.

Aortogram and Selective Coeliac Arteriography: Renal arteries and kidneys appeared normal. Splenic artery was markedly elevated, being pushed up to just below the diaphragm. Hepatic artery appeared normal. Selective coeliac arteriography showed multiple tumour vessels occupying almost the entire left abdomen, all being branches of the left gastroepiploic artery. The right gastroepiploic artery contributed branches to this large tumour mass (Fig. 2).

Barium enema: No intrinsic lesions of the colon were noted.

Liver Scan: normal.

DIFFERENTIAL DIAGNOSIS

An abdominal mass arising in the left upper quadrant can have its origin either retroperitoneally, intraabdominally, or from the peritoneum, mesentery, or omentum. A general differential diagnosis of a mass in the left upper quadrant is now given.

Retroperitoneal

(a) Tumours of mesodermal origin: lipoma, liposarcoma, leiomyoma, leiomyosarcoma, fibroma, fibrosarcoma, etc.

(b) Tumours of neurogenic origin: neurofibroma, neurilemma, ganglioneuroma, neuroblastoma, etc.

(c) Miscellaneous: teratoma, chordoma.

(d) lymphoma and lymphosarcoma.

(e) renal neoplasm or cyst.

(f) adrenal neoplasm

(g) metastatic tumour.

Intraperitoneal

(a) Tumour of left lobe of liver (primary or secondary)
(b) splenomegaly
(c) Neoplasm or cyst of body or tail of pancreas
(d) Stomach and Transverse Colon: carcinoma and tumours of mesodermal or neurogenic origin.

Omental, Mesenteric and Peritoneal

Metastatic neoplasm, mesothelioma, mesenteric cyst, lipoma, liposarcoma, fibroma, fibrosarcoma, lymphosarcoma, lymphoma.

RADIOLOGIC DIFFERENTIAL DIAGNOSIS

Provisional diagnosis was based upon radiologic investigations. Plain film and IVP: As the psoas and kidney margins were both clearly distinguishable through the density occupying the left upper quadrant, this would indicate that the mass was not retroperitoneal but either intraabdominal, peritoneal, omental, or mesenteric in origin (Figure 1). Again, the clearly outlined renal shadow and normal collecting structures would exclude the possibility of renal cyst or tumour. Carcinoma of the body or tail of the pancreas rarely reaches such proportions.

FIGURE 1—August 18, 1967. Intravenous pyelogram showing density in LUQ and medial displacement of the Left Ureter.

Upper G.I. series and barium enema: Barium enema showed no intrinsic involvement of the colon. The anterior displacement of the stomach (without mucosal involvement) seen in the barium meal would suggest the possibility of a pancreatic pseudocyst, smooth muscle tumour of the stomach wall, peritoneal tumour or mesenteric cyst.

FIGURE 2—Coelic Arteriogram demonstrating the same UI.Q mass.

Arteriography: Arteriography was used for an evaluation of the source, extent, and nature of the blood supply of the mass (Figure 2). Aortography demonstrated no abnormal retroperitoneal vessels. Selective coeliac arteriography showed a normal splenic artery, and that the mass derived most of its blood supply from the left gastroepiploic branch of the coeliac axis. The mass appeared to be malignant inasmuch it had an abundant blood supply and the vessels themselves were abnormally tortuous, irregular in calibre, and followed no anatomical direction. As the gastroepiploics supply the gastric wall and omentum, the following differential diagnosis was made.

(a) stomach wall: leiomyosarcoma
(b) peritoneum and omentum: Metastatic tumour, lymphosarcoma, malignant mesothelioma.

FIRST OPERATION

An operation was performed on August 31st. A huge, white, hard, intraperitoneal tumour fixed to the greater curvature of the stomach, spleen, and transverse colon was visualized. Secondary, similar nodules of many sizes were noted in the greater and lesser omentum. Liver had no visible or palpable nodules. Paraaortic lymph nodes were not enlarged. Resection of transverse colon with primary anastomosis, subtotal gastrectomy and gastrojejunostomy and splenectomy were performed. It was not possible to remove all the growth and there were still tumour nodules palpable in the pelvis.

The patient's post-operative recovery was unremarkable and he was discharged on September 13th. Further treatment was undecided.

PATHOLOGY

Gross Examination

The tumour mass was 15 x 17 x 12 cms, and weighed approximately 1500 grams. Its surface was coarsely nodular and fleshy in appearance. The tumour was rubbery in consistency, and on section had a gritty texture, the cut surface having a whorled fibromuscular appearance. Numerous secondary tumour nodules, identical in appearance to the primary tumour, were attached to the tumour surface.

Microscopic Examination

The tumour cells demonstrated moderate to marked pleomorphism, had large hyperchromatic nuclei with a granular, coarse chromatin pattern, an ill-defined cytoplasm, and were indistinct in outline. The cells were present in irregular cords and sheets, which were widely separated from each other by a dense acellular fibrous tissue. Areas of mucoid degeneration were noted within the acellular fibrous tissue (Fig. 3).

Sections taken from the adherent stomach and bowel showed diffuse tumour invation of the viscus wall. Sections of spleen were free of tumour.

The tumour was undifferentiated and it was impossible to be certain of its nature. Opinion favoured two main possibilities: (a) an anaplastic carcinoma originating in a malignant teratoma (retroperitoneal, or metastatic from an occult testicular primary). (b) A malignant mesothelioma. A provisional diagnosis of malignant mesothelioma was given at that time.

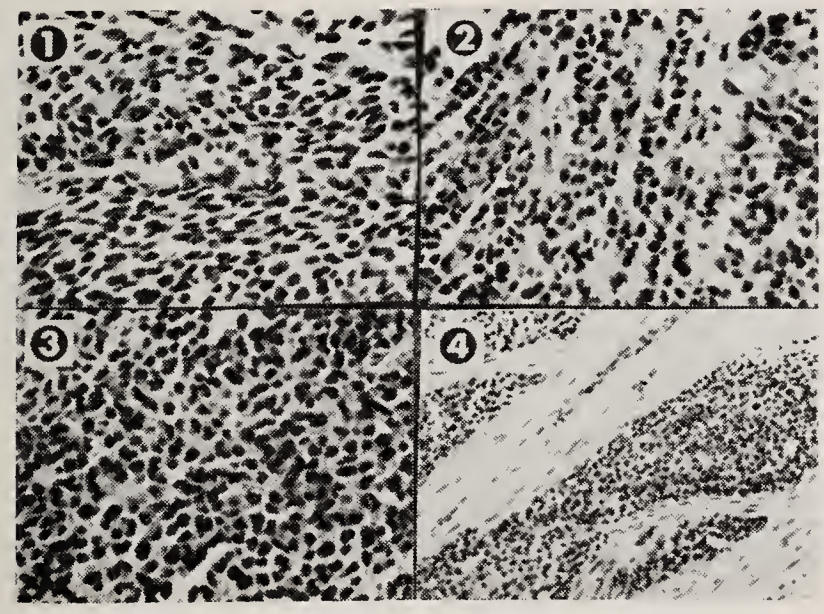

Figure 3. Microscopy of the tumour.
No. 1: Tumour showing ill-defined tendency of cells to elongate in spindle fashion. (H & E x 250)
No. 2: Tumour nodule showing cord-like arrangement suggestive of epithelial pattern. (H & E x 250)
No. 3: Tumour nodule showing indifferent arrangement of cells. (H & E x 250)
No. 4: Tumour nodule showing masses of tumour cells separated by wide fibrous stromal bands. (H & E x 100)

SECOND OPERATION

The patient was again admitted on November 25th, and he was operated upon in order to remove a large pelvic mass which threatened to obstruct his bowel. It was realized that the mass in his pelvis had grown considerably since the last operation and was not totally removable.

Chemotherapy (methylhydrazine) and radiotherapy (3500 rads) were begun on December 21st, at PMH, on an outpatient basis. Radiotherapy was discontinued in March, 1968, as there was no appreciable change in the size of the tumour mass. On April 1st he was admitted to PMH for a course of vincristine, methotrexate, and cyclophosphamide, as he had developed partial bowel obstruction and ascites. His status rapidly deteriorated and he died 8 days later.

AUTOPSY FINDINGS

Gross examination revealed extensive involvement of intestinal and stomach wall, omental, mesenteric and peripancreatic lymph nodes, and liver capsule, by masses of tumour.

Post-mortem examination failed to discover any retroperitoneal, testicular or other primary site. The tumour histology was identical to that seen at both operations, and it was considered to represent a malignant mesothelioma.

DISCUSSION — MALIGNANT MESOTHELIOMA

The malignant mesothelioma is a rare tumour arising from the cells that form the lining of the pleura, pericardium, and peritoneum. These tumours have sarcomatous growth characteristics and show multiple histological patterns within the same tumour mass, varying from the flat spindle-cell quality of the mesothelial cell or fibroblast to that of adenomatous and glandular patterns. Primary malignant mesotheliomas extend rapidly and widely over the broad surfaces, sometimes infiltrating underlying structures, and are characterized by an intractable course.

The diffuse mesotheliomas are difficult to distinguish from metastatic anaplastic carcinomas and it must be noted that some authors are skeptical about the very existence of mesothelial tumours. The association of many of these tumours (in the pleura) with asbestosis, their secretion of hyaluronic acid and the evidence from tissue culture investigations that normal mesothelial cells can produce connective tissue fibres and spindle-shaped cells, strongly indicate that the primary mesothelioma does exist. The diagnosis of malignant mesothelioma can only be made with certainty if no evidence of an alternative primary tumour can be found elsewhere.

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REFERENCES

A. P. Stout: Tumours of Soft Tissues, Armed Forces Institute of Pathology, pp. 119-121.

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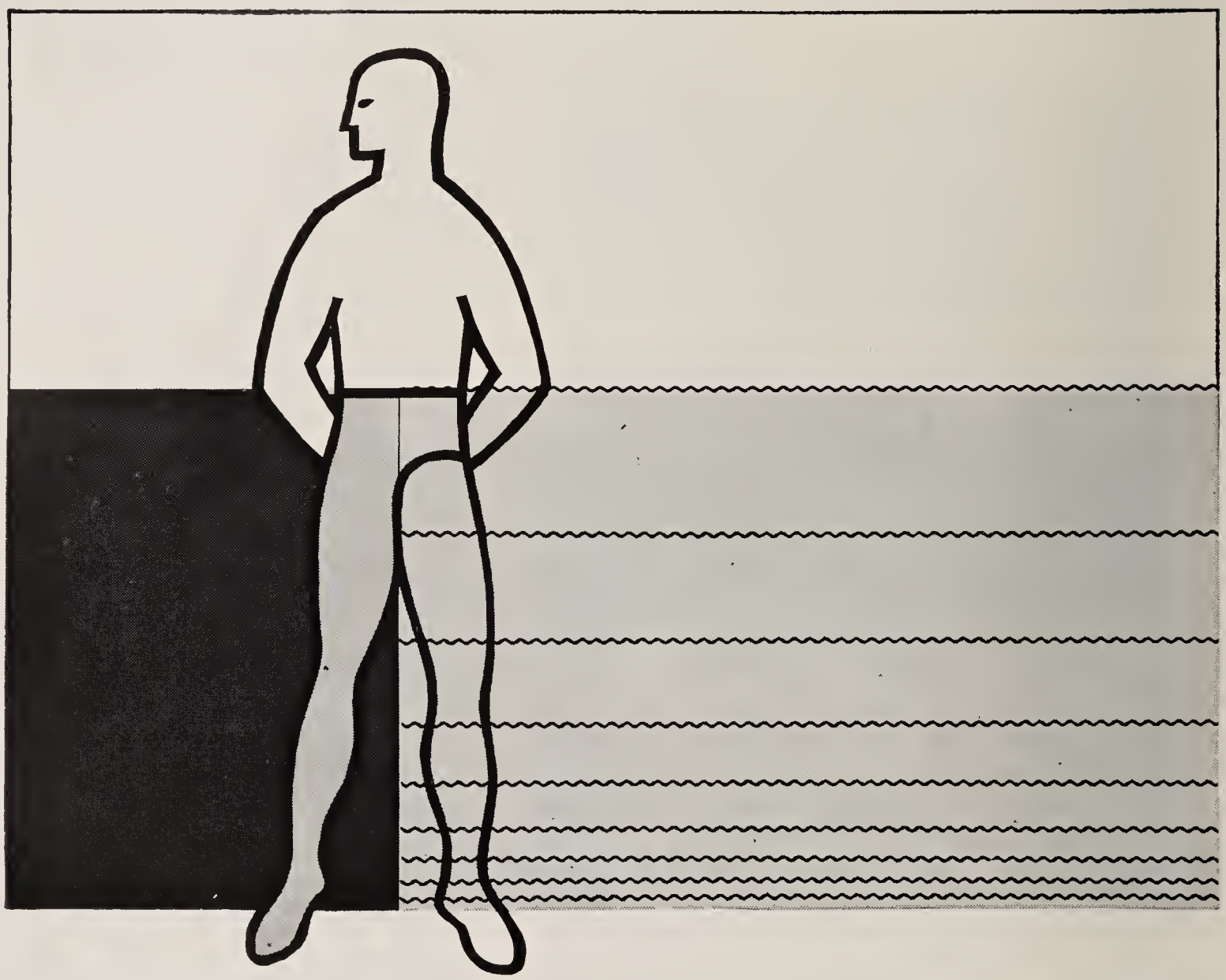

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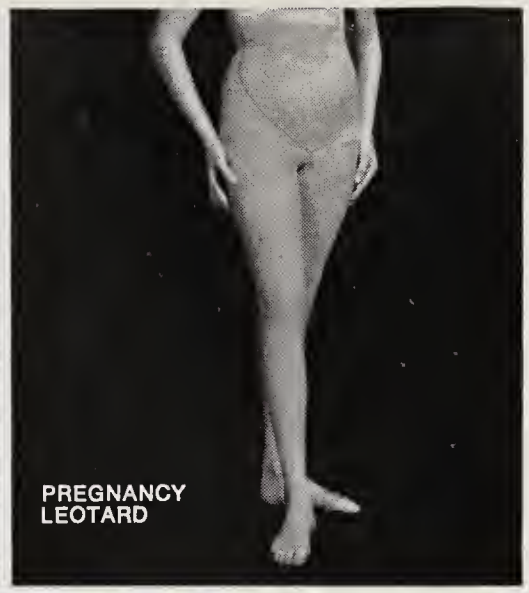

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